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ABSTRACTS & REVIEWS

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NOTICE

Owing to increases in wages and in the price of paper, the cost of production of 'Medical Science' has risen by 50 per cent. since October, 1919. The Medical Research Council have therefore been compelled to raise the price per number to Three Shillings and the Annual Subscription to Thirty Shillings.

REVIEWS

ACUTE RHEUMATISM AND RHEUMATOID AFFECTIONS

Aetiology. In an article on the specificity of acute articular rheumatism, Grenet reports having observed outbreaks of five distinct epidemics among soldiers within a limited area. The disease occurred within a zone of trenches occupied by certain regiments and also appeared in their rest camps, where they came in contact with second line troops who became infected in their turn. The immunity of a regiment after occupying the former cantonment of another regiment in which cases had occurred tended to show that contamination was not caused by the soil or by the quarters, but by direct contact. Further evidence of the contagious character of acute rheumatism is afforded by Grenet in the history of the following case. A man who had hitherto escaped rheumatism, but belonged to a regiment in which an outbreak had occurred, was suddenly separated from it and admitted to a hospital for a wound. Twenty-six days after admission he had a definite attack of acute rheumatism, and six days later two wounded soldiers occupying adjacent beds had similar attacks. While admitting that the contagiousness of acute rheumatism is of slight degree, so that it usually escapes notice, Grenet points out that it is an argument of the highest value in favour of the specificity of the disease.

Frauenthal declares that teeth and gums as sources of infection in rheumatism are overestimated, and that much harm is done by the promiscuous extraction of teeth owing to the incompetent interpretation of X-rays. Any acute or chronic infection of the gastro-intestinal canal, genito-urinary tract, or respiratory system may give rise to an acute or chronic inflammation of the joints.

According to Lambert, the percentage of acute rheumatism among the total admissions to the Bellevue Hospital, New York, has steadily diminished from 1907, when it was 2·45, to 1919, when it was 0·521. He regards dental hygiene more than any other one factor as responsible for this diminution, and thinks it probable that tonsillectomy is also in part a factor.

Symptomatology. In a series of 73 cases of rheumatic fever in soldiers, studied by White at U.S. Base Hospital No. 6, 51 per cent. gave a previous history of rheumatic fever, and 40 per cent. showed large or ragged tonsils. The joints involved in order of frequency were knee, ankle, shoulder, wrist, foot, elbow, hand, and hip. Acute pericarditis, which was usually very transient, was found in 10 per cent., and acute pleurisy in 19 per cent. There was evidence of mitral endocarditis in 40 per cent., and of combined mitral and aortic endocarditis in 8 per cent. Most of these cases were apparently of long standing. Acute temporary heart-block was found in 4 per cent.

Pemberton, in association with Robertson, Tompkins, Foster, and Buckman, made a series of studies on 400 cases of arthritis admitted to the U.S. Army General Hospital No. 9, Lakewood, N.J. 256 patients (64 per cent.) had arthritis only; 112 (28 per cent.) had a combination of arthritis and myositis; 22 ($5\frac{1}{2}$ per cent.) had myositis only; 7 (1·75) had neuritis only; and 3 (0·75 per cent.) were listed as doubtful. Exposure was the exciting factor in 58 per cent. Apparent foci of infection were present in 72 per cent., and in about 27 per cent. there was an apparent absence of demonstrable surgical foci in the head, nose, throat, teeth, or genito-urinary tract. The tonsils were most frequently the site of infection (52 per cent.); the teeth came next (33·5 per cent.); the genito-urinary tract came last (12·5 per cent.) and clearly played an almost negligible rôle in causing arthritis. 184 patients (46 per cent.) recovered in spite of the presence of demonstrable foci. This was nearly three times the number (65 cases or 16·25 per cent.) which improved after removal of the foci. The sites most frequently involved by the arthritis were the knees (62 per cent.), the ankles (35·25 per cent.), the hip (33·75 per cent.), and the shoulder (31·25 per cent.). Although many of the cases in the series had a febrile onset, probably in only a small number was this representative of what is known as acute inflammatory rheumatism. The basal metabolism was found to be normal in 80 per cent.; in 20 per cent. it was slightly below normal limits. The carbon dioxide combining power of the blood, the total fat, the cholesterol, and the calcium of the fasting blood were found to be within the normal limits. About one half of 40 cases studied showed an abnormally high value for blood-creatin. Some of these showed a decline in blood-creatin coincident with clinical improvement. There was no marked dislocation of renal function in chronic arthritis, though this function might be lowered in some cases. In a large proportion of cases there was a lowered sugar tolerance which was roughly proportional to the activity of the arthritic process. In convalescence or recovery it tended to return to normal. Recovery was apparently independent of the type of treatment employed, but was most rapid after removal of causative foci of infection. In certain severe chronic cases from which all demonstrable foci had been removed, a lowered sugar tolerance seemed to exist.

Brennemann, of Chicago, remarks that **rheumatic nodules,** which are common in England, are generally regarded as rare in the United States and in Germany. As the result, however, of careful observations during the last five years he is convinced that the nodules occur quite as frequently in his own cases as in an equal number of similar cases in England. He admits that more rheumatic nodules are to be seen in London than in New York, Chicago, or Boston, because rheumatism is more frequent in England, especially in the London district, and still more so because it is in the severe type of rheumatic infection that they attain their maximum incidence. He found that the nodules were almost always present in cases where there was severe endocarditis of long standing often accompanied by pericarditis, when the process was active and progressive in spite of treatment, and where there was a low but nearly constant pyrexia. He points out that the reason why nodules are so frequently overlooked is that one is sparing in manipulating a rheumatic patient and especially in bending the joints.

Frauenthal describes an interesting class of cases which is met with in married women between 20 and 40, and characterized by an acute inflammation of the feet and an inflammatory condition of the larger joints. The patients give a negative Wassermann reaction and agglutination-fixation test (Neisser) and repeated smears fail to show gonococci. A vaginal discharge is present and often a laceration of the cervix which causes lymphatic absorption. The joint condition in these cases is cured by vaginal douches of a solution of iodine or perchloride of mercury.

Lereboullet and Mouzon report a case of **chronic fibrous rheumatism** in a woman aged 26 following acute articular rheumatism which was remarkable for the presence of dislocations at the metacarpo-phalangeal joints. The condition was apparently caused by the looseness of the capsule and ligaments of these joints resulting from the patient's work as a dressmaker.

Versini devotes his Paris thesis to the subject of **cervico-sciatic rheumatism** which was first described by Nobécourt in soldiers in 1916. It is a form of rheumatism consisting in the association of cervical arthropathy, sciatic neuralgia, and a meningeal reaction shown by hypertension and increase of the albumin content of the cerebrospinal fluid, leucocytosis being less constant and of variable intensity. The rheumatic nature of the condition is proved by its appearance in rheumatic subjects, occasionally by the existence of other joint affections, and often by cardiac complications such as endocarditis, pericarditis, myocarditis, and dilatation of the heart. The disease is liable to be mistaken for febrile gastric derangement or cerebrospinal or tuberculous meningitis, from which it is sometimes difficult to differentiate it without lumbar puncture. Like the ordinary articular rheumatism, the cervico-sciatic form may occur independently or be symptomatic of another disease. It is found at the onset of typhoid or paratyphoid or infective jaundice, or as a sequel of antityphoid and antiparatyphoid vaccination. The prognosis is good in the simple form, but should be reserved in cases with a cardiac complication.

According to Léri, **vetebral rheumatism** is most frequently localized in the lumbar spine, where it is characterized by lumbo-sacral pain which frequently radiates to the buttocks, thighs, and legs, and by a forward inclination of the trunk. The disease is not peculiar to old persons, nearly all Léri's patients being aged from 20 to 40. Lumbar rheumatism, like every other form of chronic rheumatism, runs its course with more or less prolonged paroxysms of pain, interrupted by remissions. It is distinguished from the bent back of hysterical origin by X-ray examination, which shows various deformities of the vertebrae. Rheumatism of the dorsal spine is much more difficult to diagnose, because as a rule the X-ray picture is indefinite. In a certain number of cases, however, Léri has been able to attribute obstinate intercostal or abdominal neuralgia, and in one instance crural monoplegia, to chronic dorsal rheumatism.

Cervical rheumatism may be manifested merely by painful symptoms with or without disturbance of objective sensibility or reflectivity, or by amyotrophic paralysis simulating a primary amyotrophy, or one due to a paralysis of a peripheral nerve.

Junius, of Bonn, reports four cases of a rheumatoid affection of all the joints, including those of the vertebrae, associated with iritis. With the exception of one case in which tuberculosis may possibly have been present, the cases showed that a chronic rheumatoid condition might be produced by other infective agents than the tubercle bacillus. Even if, in view of its protean character, tuberculosis was concerned in the aetiology, the cases differed from those previously reported in the severe involvement of the vertebral joints and in the absence of any other signs of tuberculosis.

Junius suggests that cases of this kind, which are certainly rare, form a group by themselves which requires further study. Treatment was of no avail in any case.

Bittorf draws attention to a phenomenon in **muscular rheumatism** which has apparently not been previously described and has the great advantage of being the only objective sign of the disease, viz. eosinophilia. It is most pronounced in acute cases or acute exacerbations of chronic diseases, and its frequency varies from 5 to 12 per cent. of all cases. It disappears on improvement or recovery. In mild chronic cases it is much less pronounced or disappears entirely, while lymphocytosis and mononucleosis persist or become more marked. The sign is of value in distinguishing muscular rheumatism from neurasthenic, hysterical, or anaemic states, and in particular lumbago from primary chronic arthritis of the lumbar vertebrae. Bittorf's observations have been confirmed by Staeckert and Synwoldt, both of whom excluded all other diseases associated with eosinophilia such as asthma, trichinosis, and helminthiasis. Staeckert found an eosinophilia ranging from 6·5 to 16 per cent. in all his cases of muscular rheumatism. The increase of eosinophils was most marked in acute cases, and as improvement took place the eosinophilia diminished. The increase in the eosinophils was accompanied by a lymphocytosis of 30–40 per cent. and an average mononucleosis of 4 per cent. The increase in the lymphocytes and mononuclears was not, however, so constant as the eosinophilia. With four exceptions in which the blood was completely normal, Synwoldt found an eosinophilia in 19 cases of acute muscular rheumatism, the maximum being 18–22 per cent. In 11 cases of chronic muscular rheumatism the eosinophils showed the normal values of 1–3 per cent. On the other hand, in 81 per cent. of the cases there was a lymphocytosis of over 30 per cent. and in 54·5 per cent. of over 40 per cent. Synwoldt regards eosinophilia as the result of the irritation of the haematopoietic organs by the disintegration products of muscle albumin analogous to the eosinophilia in trichinosis, which, according to Staubli, is closely connected with the penetration of the parasites into the muscles and with a damage to the muscular metabolism.

Treatment. The treatment of articular rheumatism by hypodermic injection of salicylic acid is advocated by Séjournet, who uses a 1 : 1,000 solution made by pouring a litre of boiling water on a gramme of salicylic acid. 1 c.c. of the solution is injected subcutaneously in the region of the affected joint. If the pain continues, the injection is repeated the next day and the day after. It is very rare for a fourth injection to be necessary, as after four or five days the pain and peri-articular swelling subside. The chief advantages of the treatment are, first, that the patient, if treated from the onset, is almost certain to be saved from a generalization of the rheumatic infection, and, secondly, if he recovers soon, there is less chance of his heart being affected. The same treatment is successful in chronic rheumatism, gout, and sciatica, which Séjournet regards as a rheumatic neuralgia, but has no effect in arthritis deformans.

Deutsch has treated 61 cases of severe articular rheumatism in patients aged from 16 to 34 years with intravenous injections of urotropin. At first 10 c.c. of a 20 per cent. solution was used, and then 20 c.c. followed by 10 c.c. and later 20 c.c. of a 30 per cent. solution. The number of injections varied from four to fifteen; on the average seven were required. In a few cases a high temperature and rigor immediately after the injection were noted, but were probably due to the distilled water used, and subsided the following day. The only other complication was vesical irritation ranging from slight pain and frequency in micturition to well-marked haematuria. Of the 61 cases treated, 56 could be regarded as cured, as no relapses occurred after several weeks' observation. In two cases a relapse occurred after eight days, but was cured by a few more injections. In four cases the treatment was discontinued after the first few injections had produced no result.

White obtained a remarkable response to treatment in rheumatic fever with large doses of salicylates, toxic symptoms being extremely rare. His routine procedure in acute cases was to give 30 gr. of aspirin every four hours until the symptoms were relieved; usually 200 to 300 gr. were necessary in the course of two to three days to bring complete relief. The drug was subsequently continued in small doses, e.g. 10 gr. two or three times daily for a week or as long as seemed necessary.

From consideration of the results of 200 consecutive cases of tonsillectomy for myositis or arthritis, Lillie and Lyons come to the following conclusions: (1) tonsillectomy is justifiable in every frank case of myositis or arthritis; (2) a marked improvement may be assured from tonsillectomy alone in 79 per cent. of all cases; (3) all possibility of dental sepsis must be removed: by so doing a larger percentage of patients will be improved; (4) the duration of the myositis or arthritis is a factor in the ultimate results, although benefit and even complete cure is obtained in some long-standing chronic cases; (5) 40 per cent. of the patients with chronic myositis or arthritis who are invalids will respond favourably to tonsillectomy; (6) the size of the tonsil has no bearing on its possibility as a focus of infection. A careful expression of the tonsillar crypts and a history of throat trouble with the myositis or arthritis is essential in the diagnosis; (7) absence of a history of diseased tonsils in no way eliminates these organs as a focus of infection; (8) a clean tonsillectomy with removal of the plica tonsillaris is necessary in every case.

An investigation of the after-histories of patients on whom tonsillectomy had been performed at the Sabbatsberg Hospital since 1913 (chronic tonsillitis complicated by some rheumatic affection being taken as the indication for operation) has convinced Nordlund of the efficacy of this procedure in arresting the rheumatic manifestations in a large proportion of cases. Of the numerous cases operated on, he could trace only 30. These were classified according as the chronic tonsillitis was followed (1) by a single, (2) by more than one, attack of polyarthritis, and (3) by nephritis. Of the 6 cases in the first class, 4 remained well, 2 relapsed, the relapse in one of these cases not occurring till 4 years after the operation. Of the 13 cases in the second class, 10 showed no sign of relapse, although many of the patients had been subject to 3 or 4 attacks of polyarthritis every year, and the operation dated from 1913 in 4 cases, and from 1915 in 2 cases. In most of these cases the tonsillectomy was followed by a rapid fall of the temperature to normal, and by a striking improvement in the general condition. As a rule the pain in the joints abated quickly, although in some cases it did not cease completely till a fortnight after the operation. Undoubtedly the operation helped to cut short an attack of arthritis, but the ultimate results were the same, whether the operation was performed during an acute or chronic phase of arthritis, or in the interval between two attacks. Of the 12 cases in the third class there were 7 of acute haemorrhagic nephritis associated with chronic tonsillitis. In 6 of these the operation had a strikingly beneficial effect, the claim being made that permanent improvement was effected. Later, Nordland speaks of these cases as being cured. There were also 5 cases of chronic nephritis, in only 2 of which was the operation followed by improvement. While admitting that the observation period was in many of these cases too short to allow of a final judgement, Nordlund submits that his findings are strong evidence in favour of removing the tonsils when their chronic inflammation is combined with some manifestation of 'rheumatism'.

Taylor recommends thorough irrigation of the colon for myalgia. The colon should be irrigated with four or six gallons of water till the whole gut is clean. Every other day for two weeks sodium chloride and sodium bicarbonate should be added for four or five days.

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SCURVY

The following statistics are given by Willcox showing the prevalence of scurvy in Mesopotamia. During the last six months of 1916, 11,445 cases occurred in Indian troops. In 1917 there were 2,199 cases and in 1918 only 825, although the force in 1917 and 1918 had been largely increased. The maximum incidence was in the hot months of May, June, and July. Scurvy in Mesopotamia was practically limited to Indian troops. The few isolated cases among British troops could be traced to inadequate diet owing to some other disease occurring in the individual patient, e.g. dysentery, enteric and epidemic jaundice. The prevalence of scurvy in the Indian troops was due to the fact that the field service ration was very deficient in antiscorbutic vitamines, the only antiscorbutic being 2 oz. of potatoes and 4 oz. of fresh meat. The Indian soldiers were also predisposed to scurvy owing to a large percentage of them being anaemic, debilitated, and suffering from pyorrhoea. Mental depression was also undoubtedly a factor in the high incidence of the disease.

According to Comrie, who was recently Consulting Physician to the Forces in North Russia, where scurvy is endemic, scurvy of any severity was practically negligible among the British troops, the rarity among them being largely due to the inclusion in their dietary of germinated peas and beans prepared as recommended by Chick and Hume. Among the additions to the diet of prisoners suffering from scurvy which were found to be of greatest curative efficiency came in order of value soured milk, fresh meat, fresh lemon juice, germinated peas, tinned fruit, and germinated beans.

In his capacity of director of a central scurvy station of the Russian

Red Cross, Bierich was able to study 1,343 cases of scurvy in 1916 and 1917. 87·1 per cent. of his cases occurred in Slavs, 2·7 per cent. in Germans, and 10·2 per cent. in Mongolians. A previous attack of scurvy or of other diseases, with the possible exception of dysentery or enteric fever, did not appear to have any aetiological significance. Bierich regards scurvy as a reaction of the organism to a number of injurious endogenous and exogenous influences, the former consisting chiefly of racial and psychical factors, and the latter of inadequate diet.

According to Tournay, the first cases of scurvy during the war of 1914–18 occurred during the Serbian retreat. Subsequently several epidemics broke out in various parts of France. He suggests that a large number of cases of rheumatoid purpura, asthenia, haematomyelia, gingivitis, ulceration of the legs, ecchymoses, and anaemia were really incomplete forms of scurvy. He records an outbreak which occurred in a battalion of Senegalese attached to the regiment of French colonial infantry in the region north of Monastir in the spring of 1918. The earliest and most constant symptom was asthenia which, was almost invariably accompanied by pains in the limbs, especially in the ankles, legs, and knees, and in the lumbar region of the vertebral column. Petechiae and ecchymoses were difficult to distinguish on the black skin of the Senegalese, but the most definite symptom was the excessive hardness of the calf muscles. The most typical symptom of scurvy, haemorrhagic gingivitis, was much less frequent than pain in the lower limbs and was not always very pronounced. With the exception of a few cases complicated by broncho-pneumonia, similar to those which occurred in the Crimea in 1854–6, rapid recovery took place under the sole influence of rest and introduction of fresh vegetables and lemon juice into the diet.

Messerschmidt reports a small epidemic of scurvy which occurred among troops in the Carpathians. From March to August 1917 there were 31 cases, 90·3 per cent. of which were in a regiment in which the average age was decidedly higher than usual. 60·7 per cent. of the cases in this regiment came from one battalion. The mode of life of the soldiers, including their diet, was the same for all, but men over 40 were attacked in preference to others. After the introduction of green vegetables the outbreak of scurvy subsided in spite of the aggravation of other conditions. Messerschmidt concludes that other factors besides diet are concerned in the causation of scurvy, since the number of patients was very small in comparison with those who were exposed to the same injurious influences. Infectious diseases and intoxications did not appear to play any part.

According to Korbsch, during the first three years of the war no important articles on scurvy appeared, and it was only in the last two years that observations on any considerable outbreaks of scurvy were published, all of which had occurred in the Eastern theatre of war (vide *Medical Supplement*, 1918, **1**, 32, 67, 97, 218, 349; 1919, **2**, 30). On the Western front no epidemics of scurvy had hitherto been described, and sporadic cases had been so uncommon that Morawetz (*ibid.*, 1918, **1**, 218) after eighteen months on the Western front saw only one undoubted case. Korbsch now relates an epidemic of 51 cases which occurred between March and July 1915 on this front. The chief cause of the outbreak was the complete absence of the potato supply, the diet consisting mainly of rice, salted cabbage, tinned meat, and rarely containing fresh meat. Another factor was the age of the patients, all of whom were over 30 and had been on active service since

August 1914. A third factor was defective accommodation. Korbsch did not find anything to support the theory of Much and Baumbach that scurvy is an infectious disease (*ibid.* 67).

Benoit (1) describes an epidemic of scurvy which attacked 63 out of 350 men belonging to a labour corps in the north of France in May 1917. The disease was at first mistaken for peliosis rheumatica. Gingivitis did not appear till late and occurred in a variable degree in 22 per cent. A remarkable feature of the epidemic was the acute course of the disease and its tendency to spontaneous recovery, all the symptoms disappearing irrespective of the diet and in the absence of any drug treatment as soon as the patient was removed from the epidemic focus and admitted to hospital.

In the course of six weeks in 1917 Baltus saw 17 cases of scurvy in Lille. 7 of these occurred in children aged from 7–14 years, in whom the onset was most insidious, and the remainder over the age of 50. Every adult had petechiae, ecchymoses, oedema of the feet and legs, and changes in the gums of varying degree. All had pains in the lower extremities, which interfered with locomotion, together with marked weakness and anaemia. Not a single child had haemorrhage or oedema, but the gum changes were in evidence, though only to the extent of puffiness. Recovery was slow and tedious.

In an article on scurvy among the German prisoners in Russia Klein states that the first sign of an epidemic noticed was an increasing number of cases of **night-blindness.** Ophthalmoscopy showed a marked anaemia of the retina which was attributed to malnutrition. A large number of cases of obstinate conjunctivitis and bronchitis were then noticed, and several cases developed subconjunctival haemorrhages after coughing. Shortly afterwards numerous cases of gingivitis were observed, which were followed by swelling and infiltration of the lower limbs. On the other hand, in a number of cases which were often the most severe, there was no trace of gingivitis.

In a paper on the early manifestations of scurvy, based on their study of cases at a divisional rest camp in France, Pickard and Lloyd maintain that anaemia, pains in the joints and muscles, ecchymoses, swollen gums with suppuration, bleeding or loose teeth, and night-blindness, formed together the picture of scurvy in its slighter degrees and were in miniature the same symptoms that exist in the severe cases usually designated scurvy.

From a study of nearly 3,000 cases of scurvy among Serbian troops, Wiltshire found that **follicular keratosis** occurred in the vast majority of cases. In a large proportion of cases it was the first recognizable sign of the scorbutic tendency and would have enabled a diagnosis to be made before the onset of the symptoms. Its appearance was similar to the hyperkeratosis of follicles which occurs in other malnutritional states and appeared to be due to altered nutrition of the follicles produced by the simple deficiency of antiscorbutic vitamine.

A case of acute **suppurative thyroiditis** in scurvy is recorded by Bonnet in a Roumanian farmer aged 39. The pus, which showed staphylococci and streptococci, had the foul odour associated with suppurative processes in the neighbourhood of the buccal cavity. The localization of the infection in the thyroid was probably due to small haemorrhages within the gland becoming infected, which was all the more likely to occur owing to the proximity of the thyroid to the septic buccal cavity.

In a paper on the **surgical sequelae** of scurvy Ranzel describes a number of cases characterized by a flexor contracture of the knee or talipes and muscular atrophy, the condition being due to extensive haemorrhage into the soft parts and neglect of treatment. The scorbutic nature of this condition, which was recently described by Schulhof (vide *Medical Supplement*, 1918, **1**, 349) was proved by most of the cases showing residues of gingival haemorrhages and loosening of the gums, and by the condition occurring exclusively in soldiers who had returned from imprisonment in districts of Russia where scurvy was endemic.

Klein describes the following five types of scurvy, each of which is characterized by the predominance of a special group of symptoms: (1) a type in which the skin and locomotor system are principally involved; (2) a pulmonary type; (3) a cardiac type; (4) a gastro-intestinal type, characterized by loss of appetite, vomiting, diarrhoea, and intestinal haemorrhage; (5) a renal type. The first and fourth types were the commonest, and the third the rarest. The majority of cases were mixed forms, although one group of symptoms always predominated in the clinical picture. As regards prognosis the cases complicated by extensive bronchitis and bronchiolitis were the most hopeless, and the severe intestinal forms were almost equally unfavourable.

In a paper based on the study of 63 cases Benoit (2) gives the following description of the **haematology** of scurvy. The red corpuscles were always much diminished, a count of two millions being frequently observed during the first few days of the disease. In one severe case only 960,000 red corpuscles per cubic mm. were found. In mild cases the red cell count ranged from three to four millions. The diminution in the number of the red cells bore no relation to the number and extent of the ecchymoses, so that it seemed that apart from the suffusion of blood there were one or more areas in which the red cells were being destroyed. Whatever the degree of anaemia, the number of red cells began to increase spontaneously after the fifth day and reached normal in seventeen to twenty days. Poikilocytosis was very marked from the first; in more than half the cases the red corpuscles lost their discoid form. Anisocytosis was also very pronounced with a predominance of the macrocytes. Polychromatophilia was less frequently observed. The number of granular red corpuscles was distinctly increased. A count of 6·7 per cent. was not infrequently met with as early as the third day. Nucleated red cells were only found in very severe cases, and their number was always very small. The colour index was always very close to unity, either above or below. The coagulation time determined by Wright's method was not increased during the height of the disease. The same applied to the bleeding time as estimated by Duke's method. From the onset of the disease there was an increase in the number of leucocytes. The leucocytosis, which ranged from 9,000 to 16,000 per cubic mm. was definitely of the lymphocytic type. After the tenth day the number of lymphocytes gradually diminished and by the twentieth day the normal count was re-established. Investigation of haemolysins by Troisier's method showed that the serum of scorbutic patients did not possess haemolytic properties at any stage of the disease, either with regard to the patients' own red cells (autolysins) or those of a healthy person (isolysins). Cultures of the blood and inoculation into animals proved negative in every case.

Similar conclusions were reached by Castille from observations of 18 cases of scurvy, except that he often found a diminution in the number of the leucocytes, the leucopenia sometimes amounting to 1,000 leucocytes per cubic mm.

In the recent literature the question of the **infectivity of scurvy** has been occasionally discussed (vide *Medical Supplement*, 1918, **1**, 67, 256, 349). In this connexion it may be noted that the haematological findings of leucocytosis and eosinophilia correspond with those of an infectious disease. Guth suggests that the term scurvy comprises two similar diseases, one being a non-infective and purely alimentary disorder and the other an infective disease of a non-contagious nature caused by a micro-organism which finds a favourable soil for its development in a body deficient in potassium. He records an outbreak of typical scurvy which occurred in a camp of Italian prisoners between June and August 1917, 9 per cent. of the men being affected. After disinfection of the barracks and its inhabitants the epidemic ceased at once without any change in the diet, and the disease did not recur the following spring. Although the success of the measures employed did not furnish a proof of the infectivity of scurvy, they suggest that on the outbreak of scurvy in a community disinfection should be carried out so as possibly to reduce the number of cases.

Prophylaxis. With the object of providing an efficient, portable, and palatable antiscorbutic for the use of ships to take the place of preserved lime juice, which up to the present time has been a standing ration in the navy, though its efficacy has disappeared, Bassett-Smith has had prepared in tablet form a preparation which has been proved to have effective antiscorbutic properties for animals. The tablets consist of the juice of fresh lemons made up into a paste with anhydrous lactose 97 per cent. and gum tragacanth 3 per cent., each tablet containing the equivalent of 24 c.c. of unfiltered juice.

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DISEASES OF THE BLOOD

The blood in health and various morbid conditions. Rodillon describes in detail his method for estimating the chlorides in the blood, which is briefly as follows. The serum is mixed with a solution of trichloracetic acid and filtered. To the filtrate is added decinormal silver nitrate solution, then an excess of distilled water, and then an ammoniacal solution of iron alum. To this mixture is added decinormal sulphocyanide of ammonium until there is just a trace of red colour. The number of grammes of sodium chloride per litre is ten minus the number of centimetres of sulphocyanide employed. Exact formulae for each solution are given, and it is claimed that this method is at once speedy and accurate.

Chapin and Myers, on the basis of a study of 149 cases, maintain that chemical blood examinations in children are, in general, productive of results similar to those obtained in adults. The relatively greater efficiency of the kidney in the young leads to slightly lower normal figures for sugar, urea, creatinin, and uric acid, but there are no other differences of note.

The blood in old age. Billigheimer examined the blood of 60 persons (40 women and 20 men) between the ages of 70 and 90 to see if a change in the blood picture could be found in old age as the result of the privations caused by the war. The results of the examination were as follows: (1) The number of leucocytes was normal, whereas formerly they were often increased in old age. (2) The number of leucocytes was relatively increased in contrast with the polymorphonucleosis of peace time. (3) The red cells, which used to be increased at this age, were diminished in number. (4) The colour index was normal (formerly normal and diminished). (5) The albumin content of the serum was normal (formerly increased). (6) The resistance of the blood corpuscles to hypotonic saline solution was normal or even slightly increased (formerly diminished). (7) Probably the change in the blood picture due to chronic underfeeding was due to direct causes, such as absence of solid food and a watery diet, and indirectly to the action of the sympathetic nervous system. (8) The possibility of increased autolytic processes in under-nourished subjects had also to be considered.

Gamna has submitted red cells to the action of a 'saline' solution composed of 0·75 per cent. bichromate of potash acidified with 0·5 per cent. acetic acid and mixed with two-thirds its volume of saturated copper sulphate solution. In these circumstances he has seen the formation

(? extrusion) of a small corpuscular body of conical slightly globose appearance and staining deeply with eosin. A corresponding thinning of the original red corpuscle is seen opposite this body. Both bodies are enclosed in a fine envelope. He describes the staining properties of all these structures. He considers that these phenomena are significant of physical changes in the corpuscles depending on their abnormal pathological condition. He does not attempt to decide what exact functional or pathological abnormality is in question.

Pruche details experiments directed to the elucidation of problems which arise when one considers how the constitution of the blood is affected by taking large amounts of water by the mouth. It is very commonly supposed that this is passed automatically and speedily into the blood, and then eliminated by the kidneys. Pruche says that all we know of isotonicity contradicts this, as does all our knowledge of haemolysis and of the physiology of the blood. A second hypothesis is that the water is very slowly absorbed, the amount depending on the power of elimination of the kidney when about its normal work. Thus if the kidney should eliminate a unit of sodium chloride it might be possible for the blood to take up a drop of water, but absorption from the intestine would thus depend on extraneous factors. This theory Pruche demolishes by stating that he has known very large amounts of water eliminated within a few hours.

The third theory, adopted by Pruche, is that when water is taken into the intestine it is first rendered isotonic with the blood, if necessary by extraction of salts from the serum. This will be the case with pure water or hypotonic solutions. The blood serum then becomes hypotonic and excess water is forthwith eliminated by the kidney. This continues until the water is isotonic with normal serum. If a hypertonic solution be ingested a reverse progress occurs. Water leaves the vessels and so produces concentration of salts. This is corrected by the kidney eliminating excess salts, until once more the blood is isotonic with the ingested solution. He gives instances and analyses of cases in which these two processes were watched.

Walterhöfer concludes from his studies that Cabot's ring bodies and red stippling of erythrocytes are alike manifestations of the process of extrusion of the nucleus. He states that first there appears 'balling' of the nucleus and the balls of nuclear matter are thrown off into the surrounding cytoplasm. Here they are further split up, and it is in the more finely divided state that they give rise to stippling and rings as seen in films. The finely divided granules are extruded from the cell, which is then a complete normal erythrocyte. Walterhöfer has always found the abnormal forms in association with other abnormalities which are well recognized to be signs of red cell regeneration, and concludes that they only appear in the peripheral blood when regeneration is unusually brisk. He insists that they can only be demonstrated by a stain containing azure blue, and advises that Giemsa be alkalized with 1 per cent. bicarbonate to give the best results.

Arneth (1) has applied his method of differentiating neutrophil leucocytes to the lymphocyte series. He ranges the lymphocytes according to the shape of the nucleus. The four classes are: (1) with round nuclei, (2) with slightly indented nuclei, (3) with deeply indented nuclei, and (4) with indented and segmented nuclei. The last two classes include what are usually described as transitional or hyaline cells. Some authors class these as leucocytes. The proportions of the four classes are: (1) 71·4 per cent., (2) 27·1 per cent., (3) 0·6 per cent., and (4) 0·9 per cent. Arneth has also brought the size of the cells into his calculations and deduces the rule that the larger the size the less the complexity of the nucleus. In other words, a shift to the left will be accompanied by an increase of the larger cells. He does not at present attribute any particular clinical significance to alterations in the lymphocyte count.

Arneth (2) gives a very full consideration to the mast cell, and is of the opinion that it cannot be any longer looked upon as merely a variant of some other cell, but is specific in all its characters.

Arneth (3) gives the results of his studies of Türk's cells. These are also known as irritation forms, and not infrequently as lymphoidocytes or as plasma cells. Many other names have been given to these cells.

Arneth considers that we can distinguish a cell which is best called simply a 'Türk's cell', which may be large or small according to its age, and which belongs to the lymphocyte series. It occurs in various conditions, e. g. in influenza, and is not to be regarded as degenerative.

Asua (1) has studied the circumstances in which deviations of the Arneth count occur. He considers that deviations to the left occur from stimulation of the marrow, mobilizing the reserve of leucocytes, and destroying many of the adult circulating forms. Such action may be seen in acute infectious disorders. He states that deviation to the left also occurs from defect of the physiological impulse to white cell formation.

Deviations to the right occur when there is increased marrow function caused by moderate stimuli and not accompanied by unusual destruction of adult forms; this may occur in tuberculosis and possibly in syphilis. Rapid 'ripening' of myeloid cells as in goitre of the exophthalmic type may also lead to deviation to the right, as may marrow defect from any cause lowering the output of new cells while the old remain longer in circulation. Treadgold agrees with other writers in concluding that a marked left-hand shift of the Arneth count in a doubtful case, or in one previously latent, suggests active tubercular trouble. He states that 'normally production and death of leucocytes is a constant and uniform process of the body's mechanism, and the Arneth count remains constant. If, however, an infective agent can destroy more leucocytes than the body is producing, a left shift would be the result. Conversely, a greater production of leucocytes than can be destroyed at the infecting focus or foci would produce a right shift.'

Mottram and Clarke have studied the effect on the blood of radium users of the amounts of emanation to which they are exposed. These amounts are carefully estimated. They find a well-marked leucopenia, manifest after a few weeks' exposure, and recovering but slowly when exposure is discontinued. But no condition of ill health was associated with even so marked a leucopenia as 1,690 white cells per c.mm.

In a paper on blood examinations of trinitrotoluene workers, Minot concludes that the blood changes taken as a whole yield useful information as to the condition of the worker. These changes are first those of a haemolytic anaemia and later, but quite rarely, those of the aplastic type. More information as to the worker's condition is to be obtained from the red cell than from the white cell count. The paper includes a review of the work of other writers on this subject.

Johnstone has made a very careful study of the blood changes in two cases of kala-azar treated by splenectomy. In the main these are of the recognized type, viz. a sudden leucocytosis followed by slow resumption of the normal or, if the disease be not cured, of the blood picture proper to the condition. He makes a point, however, of the immediate increase of a type of cell which has often given rise to discussion. This is the so-called large mononuclear or transitional. Johnstone noted as the earliest change after splenectomy a great increase in numbers of a cell characterized by fine neutrophil granulations, a reniform nucleus with a slender chromatin network and of size almost twice that of a polymorph. He considers that this cell is intermediate between the neutrophil myelocyte and the ordinary myelocyte. He seems to have used Wright's stain, and it is the existence of many well-marked granules in cells which he would otherwise have classed as transitionals to which he calls attention. A second point of interest was the large increase in platelets with a resulting tendency to thrombosis. One of his patients died suddenly three months after operation, and Johnstone seems to think that the possibility of thrombosis cannot be overlooked.

The value of splenectomy in the treatment of kala-azar would seem to be restricted to such mild cases as may fail to react to tartar emetic. For the severe cases in which the liver is much enlarged splenectomy cannot offer any hope of more than a transitory improvement.

Sadi de Buen concludes that neither the numbers nor varieties of the leucocytes in leprosy give definite diagnostic indications. Mononucleosis is frequent, and the anaesthetic forms tend to show a larger proportion of transitional forms than normal, but there are no other changes.

Under the name of 'carotinaemia' Hess and Myers describe a new clinical picture which became apparent during some feeding experiments on children. It was noticed that two children developed a yellowish colour, similar to that of jaundice. It affected the whole body, and was most intense on the palms of the hands, where also desquamation was apparent. These two infants were taking two tablespoonfuls of fresh carrots daily, and had been on this diet for some weeks. On changing the diet the colour slowly disappeared. Two other infants on a similar diet also developed a yellow colour, but to a less extent. It was evident that the element of personal idiosyncrasy could not be left out of count. Aspirated blood showed the presence of carotin. The paper concludes with a valuable survey of work on animals dealing with allied pigmentations.

Anaemias of childhood. Meyer and Japha discuss the aetiology of the various conditions which have come to be regarded as anaemias of childhood, particularly chlorotic anaemias—oligosideraemia of some authors—and the forms with more or less splenomegaly, such as von Jaksch's pseudoleukaemia. They come to the conclusion that too much milk in the diet is largly responsible for these conditions and are not satisfied with theories of iron starvation. Funaioli deals with the pseudo-anaemia not infrequently met with in infants. A review of the literature shows that this has been referred to an actual defect in blood-volume, or to a lessened patency of the capillaries of the skin. Neither of these can be proved, and one is obliged to fall back on a nervous vasoconstrictor element to explain such cases. The blood picture is normal, nor are the children unhealthy. This pseudo-anaemia must not be confused with oligosideraemia, as is likely to be the case if the blood be not examined, and as is very frequently the case in adults. The condition often disappears when the child is able to enjoy good air, light, and food.

Aplastic anaemia. Lambri reports a case of aplastic anaemia in a woman aged 40 who presented signs of profound anaemia. Examination of the blood showed reduction of the red cells to 500,000 per c.mm., an absence of anisocytosis and poikilocytosis and nucleated red cells, a condition exactly the opposite to what is found in pernicious anaemia. There was a relative lymphocytosis. The disease, which was accompanied by a subfebrile temperature and slight recurrent haemorrhages from the gums, proved fatal in seven months. Beyond a yellow gelatinous condition of the bone marrow, the autopsy showed nothing to account for the anaemia which was the cause of death. The liver and spleen were smaller than normal.

The case of aplastic anaemia recorded by O'Malley and Conrad is chiefly noteworthy for the age of the patient, a man of 67. The blood had been examined four months before the fatal termination, and found free from abnormality of the leucocytes, and the course of the disease was probably not more than three weeks or a month. The leucocytes fell to 650. Transfusion was of very transient benefit.

Pernicious anaemia. In opening a discussion on pernicious anaemia, Colquhoun gave a very interesting historical summary, referring to the case of Combe in 1821, Elliotson in 1846, and Marshall Hall in 1854. He concluded his address with some statistics from New Zealand. These were admittedly imperfect, but interesting as showing that in 15 years in the whole of New Zealand 1,078 persons were notified as dying from anaemia, of whom 537 were males and 541 females.

Silbermann reviews the geographical distribution of leukaemia and pernicious anaemia in East Prussia. The numbers and details of cases are too few for more than the widest generalizations, but Silbermann is able to conclude that the occurrence of pernicious anaemia may be to some extent dependent on locality.

Schauman, whose earlier works on pernicious anaemia were published in 1909, 1910, and 1911, and whose material consists of 520 cases of pernicious and bothriocephalus anaemia, observed in Helsingfors in three hospitals in the period 1883–1913, devotes the present paper to the thesis that disturbances of the internal secretions, in conjunction with constitutional anomalies of the blood-forming tissues, are the fundamental causes of pernicious anaemia. Compared with these endogenous causes, exogenous causes are secondary in importance as well as in time. The similarity of pernicious anaemia to that associated with bothriocephali is, in his opinion, so great that both must depend on common primary factors, the parasite playing merely an exciting, not a predisposing part. How else, he asks, can an explanation be found for the fact that a patient, who has suffered from bothriocephalus anaemia, after a free interval of 12 years develop pernicious anaemia without harbouring the bothriocephalus? The link between the parasite and anaemia is, in his opinion, disorders of the internal secretions. He then correlates the various manifestations of pernicious anaemia with those of diseases the relationship of which to disorders of the internal secretions is already established. In this process he draws chiefly on the investigations of other workers, but he notes that since 1912, when he began to study the skin in pernicious anaemia, he has found considerable pigmentation in nine out of 64 cases. In 2 of these cases the pigmentation had extended to the mucous membrane of the mouth, and could be dissociated, with little doubt, from the administration of arsenic. With reference to the difficulty experienced in provoking alimentary glycosuria in pernicious anaemia, he gives details of 6 cases in which 100 to 200 grm. of grape sugar were given on an empty stomach without yielding a trace of sugar in the urine.

Wallgren's investigations were made at the Pathological Institute of Helsingfors University, where the tongues of 13 cases of pernicious anaemia were examined and compared with 21 tongues of healthy persons or the subjects of other diseases. He adopted the following technique: After 24 hours' fixation in 10 per cent. formalin, and embedding in paraffin, sections 7 to 10 μ were cut and stained with haematoxylin and v. Gieson's solution. Gram-staining was adopted for the study of the epithelial cells of the tongue. In 8 of the 13 cases there was a history of a burning sensation in the tongue, and in every case morbid changes in its superficial layers were demonstrable. The epithelial cells showed degenerative changes, there was proliferation of the subepithelial connective tissue, and fibroblasts were comparatively numerous. In every case there was an increase in the number of lymphoid cells in the superficial layers, and among these lymphoid cells there were leucocytes in more than half the number of cases. A characteristic feature of the tongue in pernicious anaemia is the smallness and feeble development of the fungiform and filiform papillae. These and other abnormalities of the superficial structures of the tongue account for its curiously smooth and polished appearance. Wallgren, whose investigations were largely prompted by W. Hunter's, and who compares his own findings with the latter's, admits that he failed to demonstrate inflammatory changes in the nerves. He found no micro-organisms, except in one case in which numerous cocci were seen in all the blood-vessels. But as there were no signs of a local reaction, these germs probably did not reach the tongue till the patient was moribund.

Ward (1) describes two cases of typical Addisonian anaemia at greater ages than have hitherto been described. The first was in a woman aged 86 at the time of her death, the onset having been about four years previously. The second patient was also a woman who was seen when aged 76, but of whom the subsequent history is not known. In both cases glossitis was a very prominent feature. In the first the tongue was at one time so large as scarcely to be contained in the mouth; this was before her medical attendant noticed any anaemia. In the second there were minute exquisitely tender ulcers, not only on the tongue but on the buccal mucous membrane, and even on the skin below the red margin of the lip.

Van Thienen's paper is mostly concerned with the catalase count which is a figure arrived at by estimating the amount of hydrogen peroxide decomposed by a unit of blood. Full details of the method are given. Van Thienen describes also the catalase index which is the result of dividing the number of red cells per c.mm. by the catalase count. This gives a high result in pernicious anaemia, and it is on this that the author bases his conclusion that the Addison-Biermer syndrome is a distinct morbid entity.

Redwood reports a case of pernicious anaemia in which nervous symptoms eventuating in combined sclerosis preceded the appearance of marked anaemia. At the first examination the haemoglobin was 72 per cent.

Marcora records a case in which a severe anaemia, the red cells falling to 862,000 and haemoglobin to 25 per cent., appeared to be due to infection with *B. typhosus*. The anaemia was of the haemolytic type and there was excess of urobilin in the urine. There were no gastric or nervous symptoms. During life haemoculture was negative, but a pure culture was obtained from the spleen after death. *B. typhosus* was agglutinated up to 1 in 1,250.

At autopsy no definite focus of infection was found. There were a few petechial haemorrhages in the stomach and lower ileum, but microscopical evidence was negative. The clinical signs, e.g. oedema of the bases and fever, were typical of typhoid fever.

Smithies urges 'frequent massive transfusions' in the treatment of Addisonian anaemia. In cases not greatly benefited thereby, he does in addition exploratory laparotomy, and in 53 cases has removed the spleen, gall-bladder, and appendix. In some or all of these organs he has found haemolytic streptococci. As a result, 25 per cent. of his cases have remained clinically well for from two to four and a half years; 40 per cent. have been greatly improved, and 30 per cent. have relapsed in a short time.

Anaemias of the haemolytic jaundice group. Ward's (2) paper is a contribution to the study of the haemolytic varieties of primary and secondary anaemia, and propounds the thesis that there is a group of anaemias or morbid states without anaemia characterized by (1) a tendency to familial, congenital, and/or hereditary incidence, but (2) occurring also in the form of sporadic, sometimes frankly infective, cases; (3) with an intermittent or paroxysmal course, and (4) changes in the red cells which are in most cases peculiar to these diseases, but which (5) themselves depend on prior changes in the plasma and which are (6) of a nature to render the red cells more prone to destruction, either by the normal mechanism of portal haemolysis, or by phagocytosis, or by both. With the exception of haemolytic jaundice, including both the congenital and acquired forms, these diseases are of very rare occurrence. They include Dresbach's syndrome, in which the red cells are elliptical, but there is no effect on the general health; Herrick's anaemia, which may be fatal and in which many of the red cells have a peculiar elongated or sickle shape; Malin's syndrome, in which the characteristic feature is phagocytosis of red cells and leucocytes by endothelial cells in the circulating blood, and which may also be fatal, with, finally, Clough and Richter's syndrome, in which there is auto-agglutination of red cells in the cold. This has no evident effect on the health. The paper includes reference to the pathology of this group and to its relation to other groups.

Leukaemia. Ludke considers that we cannot definitely accept the evidence adduced by various writers in favour of a toxic and infective origin for leukaemia. He prefers to suppose that various different infections may predispose to the disease, while as to the actual exciting cause we have no clue.

Chalier and Crémieu record a case of leukaemia which was peculiar in that the clinical aspect was that of the lymphatic variety. The salient features were enlargement of lymphatic glands and spleen, and widespread oedema. The blood examination (which is imperfectly reported, apparently by error) is stated to have shown the presence of leukaemia of the myeloid type. The clinical course was subacute.

Gunewardene describes a very remarkable case of leukaemia. The patient, a boy aged 3, was first seen with severe anaemia, less than one million red cells, which was diagnosed as aplastic anaemia. In five weeks he made a good recovery. He then contracted measles, and three months later was seen with a normal red cell count, no marked abnormality of white cells, but with several subcutaneous nodules on the head. Subsequently he developed the blood picture of a myeloblastic leukaemia, and died about eleven months after the apparent onset of the disease. In this case the blood picture and even the clinical findings at the time the diagnosis of aplastic anaemia was made were in accordance with what may often be seen in leukaemia, and the latter disease was evidently apparent towards the end of life. The remarkable feature is therefore the complete remission as regards the blood picture which occurred about the fifth month.

Harrison and McKelvey record the case of a man aged 29 who died of acute leukaemia seven weeks from the onset. Three weeks from the onset he developed thrombosis of the vessels of the left arm, and the autopsy revealed a large mass in the anterior mediastinum infiltrating the pleura and heart. He had little diminution of red cells throughout, but the haemoglobin is not recorded.

Munro reports a case of leukaemia which very closely simulated meningitis, and so adds one more to the multitudinous clinical pictures which leukaemia may produce. The autopsy revealed acute oedema of the brain and cord. The cerebellum and spinal cord showed leukaemic infiltration, as did many other organs.

Giulio and Siro report a case of leukaemia in a man aged 53, which is chiefly notable in that the red cells were much reduced in number, and showed the characteristics of a severe haemolytic anaemia. The patient died after a course of intensive X-ray treatment.

Macfie, who had previously reported a case of lymphatic leukaemia in which a great reduction in the number of leucocytes took place when the patient developed malaria, now records a case of myelogenous leukaemia treated by tartar emetic intravenously in a West African native who developed malaria (*P. falciparum*). A notable reduction in the number of leucocytes coincided with the appearance in the blood of the malarial parasite, but the reduction was not permanent and was rapidly effaced by treatment with quinine. The case also showed that intravenous injections of tartar emetic had no beneficial action in myelogenous leukaemia, and that such injections did not prevent the development of an attack of malaria.

Martell defines preleukaemia as a morbid condition, infrequent in adults, but less rare in children, characterized by a particular type of blood picture analogous to that of leukaemia. It is met with in those whose constitution especially predisposes them to it (e.g. in the lymphatic, thymolymphatic, and hypomyeloid states) and may arise under the influence of various aetiological factors, of which Martelli mentions syphilis, tuberculosis, malaria, and sepsis. He regards preleukaemia as a pre-agonal state, the last endeavour of the organism to react successfully. Clinically the condition is similar to that seen in von Jaksch's syndrome, infantile kala-azar, and many other severe anaemic conditions. It is the blood picture which differentiates the preleukaemic entity, and also, it must be admitted, the autopsy, for this will reveal metaplasia of myeloid tissue such as is met with in true leukaemia into which the preleukaemia may develop.

The blood picture which characterizes the condition has been many times described in individual cases, e.g. by Leube, as leukaemia, and by Ward, as secondary leukaemia. The anaemia is severe and the polymorphism of the leucocyte picture is more notable than the actual increase in white cells. There is no great preponderance of any one cell, but there are distinct signs of a myeloid reaction out of all proportion to what one might expect from any of the above aetiological factors alone. Martelli quotes cases in which the final blood picture has been frankly that of leukaemia. His paper, in effect, argues that all cases which show this blood picture are merely preleukaemic, i.e. have in them the potentiality of leukaemia

This supposition is one which the student of haematology must weigh with others in the light of the support afforded by the work of Martelli.

Sanders refers to the difficulty sometimes experienced in deciding whether a particular case is of leukaemia, and so incurable, or merely of the 'lymphocytosis of infection' described by Cabot, and so amenable to treatment. He describes a case which proved fatal, but which he puts in the latter class on the grounds that the patient had but slight increase in the number of leucocytes, but the great majority of these were lymphocytes of embryonic type.

Ravenna briefly reviews the literature which has sprung up on the subject of the benzol treatment of leukaemia since the pioneer work of Koranyi in 1912. He reports three cases. The first did well. His second case was one of tuberculosis of the peritoneum, leukaemia, and cancer of the tongue (cancer and leukaemia in the same individual is very rare indeed). The number of white cells diminished under benzol treatment, but the cancer proved fatal from malnutrition. The third case was of the acute type, and no benefit was obtained. Ravenna concludes that benzol has a distinct influence on leukaemia, as shown by reduction of white cells and increased output in the urine of nitrogenous bodies. He thinks that benzol acts as a leucolysin or by provoking a destruction of white cells indirectly, as do radium and X-rays.

Hodgkin's disease. Cantieri gives a long and interesting résumé of the present state of our knowledge of Hodgkin's disease. He reviews the evidence for a bacterial origin, and does not find that any of the hitherto described organisms can be held responsible. He details a case with typical Pel-Ebstein pyrexia. This was interesting in that the external lymphatic glands were little if at all larger than normal, while the mesenteric glands could be felt by palpation, and the spleen was enlarged to the umbilical level. An accurate description is given of the marrow changes, showing that the bone marrow was the site of quite typical lesions. This has so seldom been determined that the evidence is of importance. That there was leucopenia without eosinophilia served to make the diagnosis more obscure, and the great importance of the relapsing pyrexia in diagnosis is well brought out by this case.

Cantieri concludes his paper with details of a case which is in many ways exceptional. The patient was aged 68, and suffered from general slight enlargement of lymphatic glands and relapsing pyrexia. Hodgkin's disease was suspected. At autopsy the glands were found to show the signs of chronic irritation, but no typical Hodgkin lesions. Thus a sufficiently typical clinical picture was present in a case which could not be proven even at autopsy. Cantieri suggests that the age of the patient, which was such as one associates with atrophied lymphatic tissues, may have been the reason why the typical lesions did not develop.

Bierich has studied Hodgkin's disease and comes to some conclusions which are in advance of those already published by other authors. He states that in this disease there exist different but orderly stages of development of a specific inflammatory granulation tissue, with a tendency to regressive metamorphosis. At a comparatively early stage definite characteristic albumin destruction products are found, and these are responsible for the occurrence of local or general anaphylactic symptoms. Later, the so-called regressive phenomena occur, viz. proliferation of connective tissue, hyaline degeneration, and finally induration and atrophy of the affected structure. Bierich states that the process spreads locally by direct invasion of neighbouring tissues in the manner of a sarcoma. Alternatively it may generalize through the lymph passages and then become secondarily localized in more distant organs. From the clinical side he has been impressed with the probability that the pharynx is the site of invasion in most cases, but admits that he has no definite evidence on this point. He regards the Pel-Ebstein type of fever as certainly anaphylactic, and thus also explains the anaemia, the variation from leucopenia to leucocytosis, the eosinophilia, and skin affections. Towards the end of the paper, and before detailing some illustrative cases, he mentions that a test excision of a gland at an early stage may be useless if the granulation tissue has not yet had time to take on any of the specific characters.

Wessler and Greene have examined 25 cases of Hodgkin's disease by radiographic methods. They state that a large percentage of all cases may be expected to show shadows in the chest. These are not always typical, but two points emerge of value. First, a shadow of large size, if due to tuberculosis, is probably dense, but in Hodgkin's disease even the largest shadows are faint. Secondly, there is frequently evidence of involvement of the paratracheal glands on the right side. These glands are seldom affected in any other disease than Hodgkin's.

Porter relates a case of Hodgkin's disease in a girl aged 2 years. The onset was rapid following an acute gastro-intestinal disorder, and the retro-peritoneal and mediastinal glands were early involved. The external glands were little involved and only towards the end of the illness. The typical relapsing fever was present, and extensive involvement of the skin with pruritus was an early symptom. At autopsy marked involvement of the lungs in the specific changes of the disease was a surprising feature.

Haemophilia. Pittaluga describes a case of haemophilia, and uses it as an illustration of his classification of blood diseases. To one group he gives the name Haemodystrophias. These are (1) the haemorrhagic diathesis (2) the polycythaemias; (3) chlorosis; and (4) the eosinophil diathesis.

The case is typical and is fully described. An interesting point is the endeavour made by Pittaluga to find some characteristics in the healthy females who transmit the disease, characteristics which might show some degree of hereditary taint short of an actual tendency to haemorrhages. He concludes that the females show certain secondary characters, principally neuropathic. These are emotionalism, hyperthyroidism, and symptoms of hysteria.

In 1912 Chalier made the observation that the serum of a haemophilic added to his own blood hastened coagulation. He based on this his treatment of the case by autoserotherapy. No success was obtained. He now records a case in which he gave injections of the mother's serum with the happiest results, so that the father wrote 'Your patient is now, without doubt, better than he has ever been in his life'.

The case was a typical haemophilia with advanced joint changes, but there was no family history of similar troubles. Having had the advice of many specialists and others, he had received no benefit. Chalier found him bedridden, owing to joint changes, and suffering from severe anaemia. After eleven injections he was able to walk without support, joint swellings had notably regressed, and his general condition was much improved. Chalier recommends that 30 or 40 c.c. of maternal serum should be injected intravenously every two weeks for one to two years. At the same time he gave adrenalin, which alone had proved useless, and calcium. It is not stated whether calcium had previously been used, nor is the possible ascription of the case to the haemophilia calcipriva group dealt with, although the presence of fractures and absence of family history makes this possible.

Vines has followed up the work of Dufour, Le Hello, and others (vide *Medical Science*, 1920, **2**, 149) in treating haemophilia with anaphylactic sera. But he deliberately induced anaphylaxis in the patients, whereas the French authors did so accidentally in the first case, and thereafter used the sera of anaphylactic rabbits. Vines's results were encouraging, and when we have learnt better how to control it there is great hope, as Vines points out, that anaphylaxis may prove to be an assistance rather than a hindrance to treatment.

Purpura. Under the name of 'La dyscrasie endothélio-plasmatique chronique hémorragique' Weil groups various less well-known haemorrhagic diseases. These he regards as variants from one common picture, and this picture in its typical form he describes as follows. The patients are usually adolescent and seek advice for purpuric manifestations. Usually there is little else to note. At times epistaxis is a prominent feature, or perhaps bleeding from the gums following the friction of the tooth-brush. Rarely there is an important haemorrhage. There are two extremes of this picture, one in which the symptoms are definitely paroxysmal in incidence, and the other in which they appear continuous. From another point of view the syndrome may be subdivided, according to the chief site of manifestations, into (1) the pure cutaneous form ; (2) the ordinary form with haemorrhages from visceral and mucous surfaces added to the purpura ; (3) a large genital group including anomalous haemorrhages at puberty and the menopause. A more or less distinct sub-group is also formed by (4) those cases in which there is a distinct tendency to thrombosis of vessels, which is not infrequently hereditary. Indeed the whole syndrome may be hereditary, although this is not always the case. It is transmitted by either sex to either sex. There is tendency to recovery as age advances, but this does not commonly eventuate in entire cessation of symptoms, but rather in their general improvement.

This syndrome is characterized by certain pathological findings, of which the following are most definite, (1) absence or diminution of blood platelets, (2) failure of the blood clot to retract normally, (3) prolongation of the bleeding-time to 60 or 100 minutes, (4) the 'signe du lacet', i. e. the occurrence of petechiae in any area rendered artificially hyperaemic, as by a tourniquet, and (5) the frequent presence of varicosities or minute naevi which may rupture and be the cause of quite severe haemorrhages. Weil does not mention the syndrome of hereditary multiple telangiectases, or of familial haematuria, but these would presumably be included under the general title of 'la dyscrasie endothélio-plasmatique'.

This term Weil justifies by pointing out that the facts adduced show beyond dispute the occurrence of a syndrome characterized by two sorts of lesions, viz. of the blood and of the vessels. That the endothelium of the blood-vessels is primarily at fault rather than any other part of the vessel wall may well require more proof than is given.

With regard to aetiology no definite statement is possible, but Weil looks for an explanation rather to protein intoxication and anaphylaxis than to infective bacterial conditions.

Minkowski deals with two cases of purpura, in one of which splenectomy was performed. He favours the view of Frank, that purpura should be divided into the form dependent on destruction of platelets and the form occurring in anaphylactic diseases, the latter being due to direct injury to vessel walls. Platelets are considered to originate from megakaryocytes in the marrow, and to be eventually destroyed in the spleen. Either diminished formation or increased destruction may therefore bring about thrombopenia and so purpura. It was on this reasoning that Minkowski advocated removal of the spleen in one of his patients. The result was regarded as satisfactory; haemorrhage ceased, and there was but slight recurrence after the operation. But the case had not been followed very long when it was reported. Of other therapeutic measures, Minkowski seems to rely most on Kocher and Fonio's coagulum given intravenously.

Gordon noted in a case of purpura haemorrhagica peculiar lesions of the central nervous system, namely, extensive vacuolation strictly confined to the grey matter. He considers these vacuoles to be the result of complete absorption of cells destroyed by haemorrhages. He contrasts the localization of the haemorrhages and vacuoles with that seen in anaemic conditions, in which the white matter is always affected. He is unable to offer an explanation of this difference, but suggests that it is to be found in local peculiarities of distribution of the blood-supply.

Meyer-Estorf reports a case of meningitis with symptomatic purpura, with special reference to the blood changes. He remarks especially on the vacuolation of the leucocytes, which he found more marked in the higher classes of Arneth's classification than in the lower. From this he is led to support the contention that the higher classes, i.e. those with more convoluted nuclei, are cells of greater age. He deals with certain objections which have been urged against this view.

Cerebro-meningeal haemorrhage in purpura is a very uncommon event. Merliac, who has collected 12 cases, including one of his own in a man aged 61, states that this complication may occur at any age, and that it does not seem possible to make any individual predisposition responsible for the occurrence. In all the cases on record the patients have shown other signs of purpura haemorrhagica, such as epistaxis, bleeding from the gums, or haematuria. The symptoms vary according to the situation and degree of the haemorrhage. Sometimes death occurred suddenly, as Merliac's case. In other cases the patient develops hemiplegia, and in others again signs of meningeal reaction predominate. In acute cases the cerebral or meningeal haemorrhage is liable to occur at the onset, but in chronic cases it does not develop till later. As a rule the diagnosis does not give rise to any difficulty. Lumbar puncture as a diagnostic method should be avoided, as it is liable to give rise to fresh haemorrhage.

The prognosis is very grave, death taking place in the great majority of cases.

Erythraemia. Herrnheiser defines erythraemia as a disease dependent on interference with the mechanism by which the normal number of circulating erythrocytes is maintained. He inclines to the view that deficient destruction of red cells is responsible for the syndrome, but advocates further research. He records a case in which there was orthostatic albuminuria and hypoplasia of the heart and aorta (by X-ray examination), but no increase in size of the spleen. The highest red cell count was 7,800,000, and was noted after venesection; on admission and before treatment the count was

6,350,000. The symptoms were those usually seen in more marked cases of the disease, viz. intense headache, fatigue, giddiness, &c.

Santos deals with the various forms of polycythaemia. He excludes from the group of simple primary polycythaemias the following compensatory forms: (1) cardiopathic, congenital, and acquired; (2) toxic (arsenical); (3) pulmonary; (4) associated with duodenal ulcer; (5) associated with chronic pancreatitis; (6) due to tuberculosis of the spleen; (7) premenstrual; and (8) the polycythaemia of high altitudes. Of these he gives an illustrative case associated with duodenal ulcer in a man of 34, the red cells reaching 7,220,000 per c.mm. and a cardio-respiratory case.

The types of polycythaemia in which the increase of red cells seems to be primary, Santos divides into two groups, the first with, and the second without, splenomegaly. The first group contains the ordinary Vaquez type and the von Descatello type, which differs only in having an associated high blood-pressure. The second group contains the Geisbock type with high blood-pressure, the Blumenthal type with myeloid changes in the blood, and the Arnstein type in which neither of these are present. These two groups are included under the name of primary simple polycythaemia, and have as common features, redness of the skin and increase of the red cells.

The interest of the paper lies largely in the illustrative cases, one of which had the rare symptom of blood-stained saliva. Santos does not mention Ayerza's syndrome of polycythaemia due to fibrosis of the lungs, but it would presumably fall into his third class of compensatory polycythaemias.

Asua (2) advances a classification of polycythaemias based on pathological rather than clinical grounds, but he deals mainly with syndromes which Santos would include as primary polycythaemias. Asua makes two main classes: (1) due to diminished haemolysis, and (2) due to increased haemogenesis. Diminution of the normal activites of the spleen, e.g. in tuberculosis of that organ, is the only cause of diminished haemolysis recognized. Increased haemogenesis occurs in the Vaquez-Osler disease, as to which Asua makes no new suggestion. It also occurs under the influence of various exciters of bone marrow function, e.g. haemorrhage, haemolysis, possibly nervous influences, and endocrine disturbance. Under one or other of these headings Asua would include all non-compensatory polycythaemias. He gives cases and discusses the increased resistance to saline haemolysis in a case of asplenia associated with moderate increase of red cells, viz. 6,500,000. It is to be regretted that we are not as yet agreed as to the normal count at each age period, for it is not every author who would regard these figures as evidence of polycythaemia.

Warthin describes as 'A case of Ayerza's disease' a case of the syndrome to which the name polycythaemia vera or erythraemia is commonly applied. Ayerza first demonstrated the association of this syndrome with an atheromatous sclerosis of the pulmonary arteries, commonly of syphilitic origin. There are certain points which should permit a differential diagnosis between erythraemia and Ayerza's disease, so that it is improbable that all cases of the former depend on pulmonary sclerosis, but there is no doubt that many cases of this sort have been too hastily identified with erythraemia in the past. Warthin's paper claims to describe Ayerza's disease for the first time in the English language. It is also interesting from the fact that Warthin expresses his categorical opinion that there is no such thing as a primary polycythaemia.

Friedenwald gives a summary of the optic and visual disturbances which have been described in polycythaemia vera. He adds a case in which marked changes were present, but there is in this particular case very little to substantiate his diagnosis.

A case of erythraemia associated with erythromelalgia is recorded by Redlich in a man aged 35, the attacks of erythromelalgia being brought on by warmth, effort, or letting the legs hang down. Similar cases have been reported by R. Schmidt, Türk, Parkes Weber, Schmilinsky, Weintraud, Gstrein, and Singer.

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G. W.

PLASTIC OPERATIONS ON THE THUMB

The loss of the thumb at or about the metacarpo-phalangeal joint, whilst the mobility of its metacarpal is preserved, has suggested the restoration of the lost projecting portion, which can then be opposed to the index or other remaining finger. A man may thus be able to clutch and move a lever, a woman to hold sewing, whereas, left alone, the damaged hand is of no more use than a stump.

There are, however, objections to attempting plastic surgery in such cases. The best that has been achieved hitherto has been a rigid prolongation of the metacarpal, which when opposed to the finger has a very feeble power of grasp, and even that amount of gain has been considered the exception. To attempt a re-formation of the thumb immediately upon the injury has been held dangerous owing to sepsis which may spread to the arm. Only after healing has been completed and then after a further period of six months is it deemed safe to proceed.

During the time which elapses after the injury, the patient has developed additional use of the sound hand. If a plastic operation is then undertaken he has to face another and more prolonged period of hospital treatment and will be prevented from returning to his former occupation or some modification of it. Meanwhile the forearm and arm on the side of the damaged hand are perforce kept at rest and the muscles become wasted from disuse. Even when the graft has united the arm easily tires and cramp is felt. It is not only the union of the graft with the metacarpal that is required, there is also the restoration of the circulation through the graft. This is very slow in becoming adequate, and meanwhile the graft remains cold; it may at any date undergo dry gangrene and drop off. The return of innervation is slower still. During the two years following the operation, the zone of innervation advances from the base of the graft towards the tip, and during this time trophic ulcers and necrosis may endanger the vitality of the graft.

Two methods which have been tried for the restoration of the thumb were introduced by Nicoladoni of Graz. In 1896 he fashioned a pedunculated flap raised from the skin of the thorax into a cylinder and applied this cylinder to make a cap for the stump of the thumb. After healing of this cap with the end of the metatarsal, he stiffened the cap by inserting a bone graft. In 1898 he replaced the lost tip of the thumb by the man's second toe. A third method is to shift a finger across to serve as a thumb, which was commenced by Muskat. A fourth method employs skin-flaps from the hand.

Concerning the first method, Schepelmann has published a full account extending over 4½ years from the operation, together with conclusions drawn from his experiences.

Former efforts have afforded very little increase in earning capacity. After prolonged treatment, it is 2–3 years before any conclusion can be reached concerning the functional result. Bones and soft parts have to take up fresh movements, blood-vessels and nerves have to re-form. Before these have become sufficiently established, trophic ulcers and sequestra may develop. There is a loss of occupation for the time and a long course of treatment in hospital. Thus patients and others tend to oppose the undertaking. There may be much preliminary difficulty in bringing the hand into use after the completion of the plastic operation. Patients have even demanded the removal of the graft because they found it in the way, as in cases of a stiff finger.

Schepelmann's case met with an accident in November 1912. He was then aged 17; he lost the thumb of his right hand at the metacarpophalangeal joint, also the middle finger at the same joint, and the ring and little finger at the base of the corresponding metacarpals. The index finger alone remained uninjured. Schepelmann formed an end to the first metacarpal by a roll of skin from the abdominal wall and later inserted into it a section of the boy's fibula, which became ankylosed to the end of the metacarpal. Whilst the operation succeeded so far as the union of the graft, there was trouble from bone sinuses and trophic ulcers; there was a puckered abdominal scar which was painful, and pain was felt in the leg and ankle consequent on the removal from the fibula. 4½ years after the plastic operation, the patient complained of cramping pain in the leg and pain and pressure upon the abdominal scar. In winter the implanted thumb became blue, cold, and swollen with pain at the junction of union with the stump of the thumb. The right arm soon tired and he used for most things his left, his right only for such light use as writing and eating. The preserved index finger could touch the tip of the grafted end of the thumb. There was sensation in the proximal half, but the distal half and tip of the graft was still insensitive; there had been, however, no recurrence of trophic ulcers for 2½ years. The original length of the graft had been 5 cm., but it had been reduced by sequestration to 4·3 cm.

The compensatory allowance for two years after the accident had been 75 per cent. of his earnings; following upon the formation of a projecting thumb the allowance was reduced to 60 per cent. For the last year he had obtained work as an engine-driver on a quarry railroad at 4 marks a day. Schepelmann considered that the compensatory allowance might be reduced to 50 per cent. and ultimately to 40 per cent.

In carrying out this method the hand is kept fixed to the wall of the chest or abdomen until it is safe to divide the pedicle of the skin-flap. The bone to stiffen the cap has been also taken from the tibia, or crest of the ilium, or a metacarpal or metatarsal bone has been transplanted.

Arlt reported that a soldier had the thumb, index and middle fingers blown off at the metacarpo-phalangeal joints. Three months afterwards a roll of skin was fashioned from the chest to form a projection for the thumb, and 6 months later this was stiffened by the insertion of the second metacarpal. The result was a projection corresponding in length to the proximal phalanx, which could be moved by the first metacarpal and which could oppose the remaining ring and little finger.

The second method makes use of a toe; the great toe because of its size; the second toe has proved too small. The objection to the method is the necessity of keeping the hand fixed to the foot for so long, until it is safe to divide the pedicle. To attempt a free graft is to court failure.

Lambert exhibited a case two years after the operation and considered the loss of the phalanges of the great toe of no importance.

A boy aged 13 was handling a bomb when it exploded and blew off the thumb and fingers of the left hand through the proximal phalanges. There remained half a centimetre of the phalanx beyond the metacarpo-phalangeal articulation of the thumb. The stumps of the phalanges healed over in two months. Then Lambert proceeded to expose the remaining bit of the first phalanx of the left thumb, and to apply to it the distal portion of the proximal and second phalanx of the right great toe. The boy was fixed by plaster bandages in such a way that the left hand was held in apposition with the right foot, whilst the left shoulder was fixed so that it could not separate farther from the right lower limb. The right upper extremity and the left lower extremity remained quite free. At the first operation the long extensor tendon of the great toe was cut through and its distal end united to the radial aspect of the stump of the thumb ('suturé avec le bout proximal de l'extérieur du pouce'; Lambert does not say 'sutured to the proximal end of the long extensor tendon of the thumb'). The pedicle chiefly consisted of the external and plantar tissues supplied through the terminations of the dorsalis pedis and external plantar arteries. Five days after the first operation 1·5 cm. of the pedicle was cut through; eight days after the outer part of the pedicle containing the main blood-supply was divided; nineteen days after the operation all the pedicle was cut through and the plaster removed. Then the distal ends of the flexors of the great toe, together with the skin, were sutured to the corresponding surface of the thumb ('on recherche les tendons fléchisseurs, on les suture ainsi que la peau à la face palmaire'. Here again Lambert does not say that he sutured together the flexor tendons of the thumb and great toe.) A slough followed on the palmar aspect of the graft, from which a bit of flexor tendon was discharged and healing followed. Six weeks after the grafting a zone of innervation 1 cm. in depth was noted on the dorsal aspect of the base of a graft; at the same time a trophic ulcer appeared near the tip, which extended to the bone, from which a small fragment was exfoliated. Sensation reached the end of the graft eight months after the operation, when the graft could be moved upon the metacarpo-phalangeal point. Two years after the operation the boy was working as an apprentice in an automobile workshop. The photographs show full movement of the thumb at both the carpo-metacarpal and the metacarpo-phalangeal joints, not in the interphalangeal joint of the graft itself. But by movements of the former two joints the end of the ingrafted toe could be opposed to all of the finger-stumps. The objection raised against the cramped position whilst the hand is fixed to the foot did not apply, owing to the patient being a boy; without causing displacement he was able to get out of bed and drag himself about the ward. The graft had at first been larger than the uninjured thumb, but the latter had grown in the meantime and now the two were about equal. The gait had not been affected by the removal of the end of the great toe. As a sign of use the palmar aspect of the graft presented a callosity caused by holding a tool. Whilst some of the distal phalanx of the graft had been lost by necrosis, yet the nail remained.

The third method consists in transferring a finger, generally at a secondary operation, selecting a finger which is relatively of little use. But it is possible to adopt the plan immediately on the injury, for Schmiedt carried this out on a soldier whose right hand had been injured by the explosion of a hand-grenade. The thumb had been blown off at the metacarpo-phalangeal joint; the index and middle fingers were uninjured; there was a comminuted fracture of the proximal phalanx of the ring finger which had left the tendons uninjured; the little finger had been lost like the thumb. Five hours after the injury the wound was cleansed and the ring finger drawn across the palmar aspect and the raw surface at its base sutured to that left by the blowing off of the thumb. The bridge was divided 17 days later, and, by the aid of suitable splinting, healing occurred in six weeks. There was then, in place of the phalanges of the thumb, the two distal phalanges of the ring finger, placed a little to the ulnar side of the normal position of the end of the thumb. There was a joint between it and the metacarpal, and the man was able to oppose it to the index finger and grasp feebly. Unfortunately the patient was soon afterwards killed by a shell.

Machol also succeeded in making use immediately of this method. The man had lost the right thumb through the metacarpal just proximal to its head, also the middle finger through the distal part of the first phalanx. The third metacarpal was cut across near its base and, preserving a palmar and dorsal bridge including the tendons, it was shifted across the palm, so that the distal half, including the head of the third metacarpal together with the stump of its first phalanx, was fixed to the end of the remnant of the first metacarpal. The extensor tendons of the middle finger were united to the abductor pollicis tendons. The bridges were divided 16 days after. Some sloughing followed; seven months later there was a movable end to the thumb, somewhat shorter than the length of the normal first phalanx. The illustrations show the man making use of this in sharpening a pencil, picking up a small object between it and the tip of the index finger, holding a pen between the index and ring finger whilst the shank of the pen was steadied between the restored thumb and the index finger, also unbuttoning his tunic by pressing with the tip of the thumb formed by the stump of the first phalanx of the middle finger.

The method at a secondary operation is to transplant a useless finger. This was adopted by Luksch in 1903 for a man who had a stump of a thumb projecting half an inch; he had also lost the tip of the index finger and the interphalangeal joint was stiff. The damaged index finger was transplanted on to the stump of the thumb. This procedure was followed by Hueck for a boy aged 12 who was handling a hand-grenade when his thumb and first two fingers were blown off, leaving a useless and stiff ring finger as well as an uninjured little finger. The base of the ring finger was mobilized, shifted across, and applied to the stump of the thumb. The result was that he was able to hold a lead pencil, spoon, or knife, and had sensation in the transplant.

Manasse combined the two methods. A soldier had his right hand injured by an explosion in November 1917. After healing, the thumb presented a bit of the first phalanx mobile on the metacarpal; the same was the case with the index and middle fingers. The ring finger was stiff, somewhat over-extended at the metacarpo-phalangeal joint, and slightly flexed at the interphalangeal joints, also it continued painful. The little finger retained some movement, but was flexed obliquely under the ring finger. Hence the hand was useless. The stump of the thumb was lengthened by a roll of skin from the abdominal wall, stiffened by a strip of bone from the crest of the ilium. The painful and useless ring finger was transferred to the mobile end of the stump of the first phalanx of the middle finger and it united so that there was flexion through 50° from full extension. The patient was exhibited immediately after healing.

A fourth procedure is exemplified in the case described by Ombrédanne.

A girl of 20, when a year old, had had the thumb and fingers of the right hand burnt off, so that there was left a rounded stump, flattened anteroposteriorly with a slight projection of the second and third metacarpals. Within the stump, the first metacarpal had retained separate mobility. The plastic operation consisted in separating the first metacarpal whilst preserving its muscular attachments. A dorsal and a palmar flap of skin were raised so as to expose the attachment of the adductor pollicis, which was freed from the 2nd and 3rd metacarpals by blunt dissection. This was done whilst avoiding interference with the carpo-metacarpal articulations. The skin covering the outer aspects of the first metacarpal was carefully protected; the irregular bony projections of the second and third metacarpals were excised subcutaneously. Then the skin-flaps which had been raised could be so fixed down as to cover in and form a web between the first and second metacarpals. The first metacarpal was thus rendered mobile, and it could be adducted towards the palm so as to close the fold between it and the second metacarpal. After healing, there was a stump of the thumb measuring 4 cm. in length, and although lacking in sensation on the palmar aspect it could be opposed to the rest of the stump-like hand. The girl had grown up to use the left hand; as a result of the plastic operation, she gained the power of holding her sewing whilst stitching with the left hand, also she could turn a leaf of a book and hold her knife to cut her food; also she could hold a pen and learnt to write, all with the right hand.

Verrall described three cases of reconstruction of the thumb.

Case I. There was a loss of the thumb at the metacarpo-phalangeal joint, of the index finger at the carpo-metacarpal joint, the middle finger was partly flexed and ankylosed, the ring and little fingers were preserved. The first metacarpal was mobilized by raising a skin-flap and excising scar tissue whilst preserving the opponens muscle. The skin-flap was then brought down so as to make a covering for the web. The man was able to oppose the first metacarpal to the tip of the flexed middle finger as well as to the mobile ring and little fingers.

Case II. The thumb had been lost at the metacarpo-phalangeal joint, the index, middle, and ring fingers through the proximal phalanx. The second metacarpal was divided behind its head, which, along with the metacarpo-phalangeal joint and the stump of its proximal phalanx, was shifted across with its flexor and extensor tendons and fixed on to the end of the first metacarpal. After healing, the man regained a movable joint, in the position of the normal first metacarpo-phalangeal joint, so that he was able to hold a pen between the restored thumb and the little finger.

Case III. The thumb was lost at the middle of the first metacarpal, the index and middle fingers at their metacarpo-phalangeal joints. The proximal half of the second metacarpal was excised and used as an intramedullary graft, one end inserted into the end of the first metacarpal. Upon this was fixed the distal portion of the second metacarpal, and thus a thumb was fashioned between which and the ring and little fingers the man could grasp a stick. The flap of skin raised to expose the first and second metacarpals was fixed down to form a web across the space between the newly-constructed thumb and the rest of the hand.

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LESIONS OF THE VAGUS AND NEIGHBOURING NERVES

The war furnished a number of instances of men wounded by bullets and fragments of shell about the base of the skull who escaped death from haemorrhage. At varying periods after the injury there were noted in these cases concurrences of symptoms, syndromes, indicating lesions of the roots and branches of the pneumogastric and neighbouring nerves. A review of such cases supplies information confirming and supplementing previous observations concerning physiological action, the location of the lesion, and prognosis. In connexion with prognosis it is necessary to distinguish the effect of compression by haemorrhage from that of complete division; the former is likely to be partial and transitory, the latter total and persistent. Among the various functions of the vagus, the one which has the least tendency to recover after paralysis is that of the vocal cord. Of adjacent nerves, damage to the auditory is mostly permanent. There is little opportunity for active treatment; except as just noted, a slow improvement may be generally anticipated to occur spontaneously. The locality of the injury is often a contra-indication to a surgical exploration. In the neck there may be some opportunity for neurolysis. In the one case in which suture of a recurrent laryngeal nerve is reported to have been followed by improvement the nerve had apparently been only incompletely divided.

A review of some of the published cases of gunshot injury helps to explain symptoms following fracture of the base of the skull, or extension of suppuration from the ear, or enlargement of glands in the neck.

The anatomical relations and communications of these nerves are complex in the extreme. Names have been attached to various syndromes, but confusion is thus introduced because of the minor variations in the several cases.

Allusion is made below, first, to the distinguishing lesions of the glossopharyngeal, pneumogastric, accessory, cervical sympathetic, and abducent nerves; secondly, to the cases illustrating groups of symptoms.

The **glossopharyngeal nerve** may be injured apart from the pneumogastric, because in the jugular foramen it is separated from the pneumogastric by the inferior petrosal sinus, and whilst running in a groove of the petrous bone it is enclosed in a fibrous canal. In a fourth of the cadavers examined by Partridge this canal was found to be bony.

The highest roots which emerge from the brain immediately below those of the facial arise from the upper end of the ventral nucleus of the vagus. They have been traced past the jugular and petrosal ganglia as motor fibres to supply the stylopharyngeus and the superior constrictor of the pharynx. Beevor and Horsley, in 1888, said that excitation of these roots in the monkey caused also a contraction of the middle constrictor. On the other hand, in 1892 Rhethi and in 1897 Kreidl concluded that only the stylopharyngeus was supplied. According to Vernet, the superior constrictor pushes on the bolus of food by diminishing the lumen of the pharynx, whilst the stylopharyngeus with the middle and inferior constrictors draw up the pharynx and shorten its length. The signs which distinguish a paralysis of the glossopharyngeus, apart from the accessorius, is that in the former case swallowing requires more than one gulp, for the throat seems too small, as if hindered by something pressing on its back wall. There is a spasmodic cough, the larynx is irritated by the check in the descent of the bolus. On depressing the patient's tongue and touching the back wall of the pharynx with a probe, so that he makes a swallowing movement, the pharynx on the paralysed side is seen to be drawn over and upwards towards the sound side. This has been described as like the drawing across of a curtain. According to Vernet it is the sign that the superior constrictor is supplied by motor fibres through the glossopharyngeal. The sensory fibres of the glossopharyngeal originate in the jugular and petrosal ganglia; the central fibres pass to the fasciculus solitarius and the surrounding grey matter; the peripheral fibres form connexions with nerves belonging to the 5th, 7th, 10th, and sympathetic. There is general agreement that the glossopharyngeal nerve supplies common sensation to the mucous membrane of the posterior third of the tongue behind the V formed by the circumvallate papillae. There is still doubt as to whether the glossopharyngeal is the nerve of taste. It has been stated that division of its intracranial roots causes complete loss of taste, as well as atrophy of the taste buds. In testing for taste, it is noted that sweet, acid, and salt sensations are chiefly perceived on the anterior two-thirds. Bitter sensations (quinine, aloes) are not well perceived near the tip of the tongue, but are especially well recognized on the posterior part. Assuming the glossopharyngeal to be the nerve of taste, it supplies the lingual nerve through its tympanic branch of Jacobson, the small deep petrosal and otic ganglion. It supplies the chorda tympani through the nerve of Jacobson, the tympanic plexus, the lesser petrosal, and the geniculate ganglion on the facial nerve. In confirmation of this view, the division of the root of the 5th nerve, as well as the excision of the whole of the Gasserian ganglion, in the course of the operation for the relief of trigeminal neuralgia, does not cause loss of taste, either at the tip of the tongue or on the soft palate or fauces. By its tympanic branch of Jacobson the nerve supplies sensation to the middle ear including the fenestra ovalis and fenestra rotunda, the mastoid antrum, the Eustachian tube; also, by its pharyngeal and tonsillar branches, sensation to the nasopharynx and posterior pillar of the fauces. There is overlapping with the pneumogastric both in the ear and in the fauces. Vasomotor and secretory disturbances have been described in connexion with the glossopharyngeal which are due to its communications with the cervical sympathetic.

Vagus, pneumogastric or 10th nerve. The intracranial roots of the vagus form a flattened band of twelve to fifteen filaments between the glossopharyngeal roots above and bulbar roots of the accessory below, lying behind the choroid plexus and floculus and in front of the occipital bone. The motor fibres are derived from a dorsal column of small cells and from a ventral column of large cells, called the nucleus ambiguus. The fibres are mainly small, and their actual distribution seems to be to the unstriped muscle of the bronchi, oesophagus, and stomach.

The sensory nerves are derived from the two ganglia, the jugular ganglion of the root in the jugular foramen and the cervical ganglion of the trunk. These ganglia are of the spinal type, the cells unipolar. The central branches ascend to form a large part of the fasciculus solitarius.

The auricular branch of Arnold derives its fibres from the upper, jugular or ganglion of the root, and is distributed in a circle 3–4 cm. in diameter with the external auditory meatus as a centre. The lower cervical ganglion of the trunk supplies fibres to the pharyngeal and superior laryngeal branches. The sensory fibres of the soft palate run with the motor fibres from the pharyngeal plexus. The sensation of the hard palate is through the fifth nerve. Disturbance of sensation may give rise to hyperaesthesia when simple pressure may cause cough, e. g. on that side of the thyroid cartilage, or behind the angle of the jaw. There may be tickling or constriction or pain in the pharynx. A spasmodic cough like whooping-cough may be spontaneous, owing to disturbance of sensation over the glottis. Disturbances of secretion, salivation, or dryness show that the sympathetic fibres running with the pneumogastric fibres are involved.

In order to relieve the gastric crises complicating tabes dorsalis, Küttner tried the effect of dividing the pneumogastric roots on one side. A wide removal of bone so as to expose the left cerebellar fossa was done at the first operation, and at the second, ten days later, the lateral sinus was ligatured, the lateral lobe of the cerebellum retracted, and the roots of the vagus divided, without disturbance of the accessorius. The patient after the operation had a free discharge of cerebrospinal fluid; later the fistula became septic, and death followed after five weeks. There had been no relief from the gastric crises by this unilateral operation.

The accessory or 11th nerve. This nerve has been proved to be developed as a caudal extension of the vagus and is not an independent nerve. The bulbar roots, mainly of small fibres, form 5-6 bundles; the spinal roots, mainly of large fibres, are distributed exclusively to the striped muscle of the sternomastoid and trapezius and are closely connected with the upper cervical nerve-roots, especially the 1st cervical. The bulbar roots of the accessory join the vagus beyond the ganglion of the trunk; the spinal roots merely adhere and can be freed by dissection. After joining the vagus the bulbar roots have been traced to supply in the soft palate the levator palati and the azygos uvulae, the middle and inferior constrictors of the pharynx, the crico-thyroid through the external laryngeal, also the cardio-inhibitory fibres. The rest of these fibres constitute the recurrent laryngeal nerve.

As to the cardio-inhibitory fibres recent experiments by Schafer prove that the sympathetic has no share. Even so long as two years after an excision of a length of the vagosympathetic from one side of the neck of a dog or cat, excitation of the peripheral end has no effect on the heart. This excludes any regeneration of cardio-inhibitory fibres from the cervical sympathetic low in the neck.

The **oculo-cardiac reflex** was found by Petzetakis to be a means of distinguishing an injury of the pneumogastric in the neck from that of the recurrent laryngeal at the same level. When in the dog the eyeballs are compressed there is a slowing of the rate of the heart-beat by as many as 20–30 beats a second. In man there is a diminution of the beats of the heart by 5–10–15 a minute. When, beforehand, the spinal cord is divided in the dog at the level of the last cervical vertebra, the opposing stimulus of the accelerator centre is cut off and, the cardio-inhibitory effect being now unopposed, the result of compression of the eyeball is to arrest the heart for 10–15 seconds or to cause arrhythmia and extra beats, owing to a disturbance of the auriculo-ventricular nervous mechanism. The oculo-cardiac reflex is lost after the injection of atropin, but then the unopposed accelerator influence cannot be distinguished from the effect of the atropin upon the ends of the pneumogastric. Collet and Petzetakis described five cases of soldiers wounded by fragments of shell. They had been seen and examined within a month of the injury and were subsequently watched for months. There were instances of injury to the pneumogastric about the level of the larynx, so that the hypoglossal nerve to the tongue and the accessory fibres to the soft palate and pharynx were intact. There was paralysis of the vocal cord on the injured side and an acceleration of the pulse to 100–135 with instability of the rate, so that there were sudden variations down to 70 a minute. On the side not injured the oculo-cardiac reflex was markedly increased. When the eyeball of the uninjured side was compressed the heart-beat might be arrested or there was arrhythmia with extra beats. On the other hand, the compression of the eyeball on the side of the injury produced a slight acceleration by two or three beats. If the paralysis of the vocal cord tended to improve, so the oculo-cardiac reflex showed signs of returning.

The centripetal course of the reflex was traced through the ophthalmic division and main root of the 5th nerve, the centrifugal course along the vagus in the neck and down the spinal cord to the highest dorsal roots.

Achard and Binet noted that compression of the eyeballs caused in addition a slowing of the respiratory rhythm, even a temporary apnoea; simultaneous effect on the blood-pressure is a variable one.

The functions of the afferent fibres of the vagus in regulating the rhythm of respiration have been rendered doubtful. Schafer found that the effect of dividing both vagi in the neck simultaneously was mainly due to asphyxia. This is more marked in young animals because the cartilaginous larynx yields and the rima glottis collapses under the influence of the vacuum produced by inspiring. In older animals the greater rigidity of the larynx diminishes somewhat the effect of inspiratory suction. The slow, deep respiration which follows bilateral vagotomy is obviated by a preliminary tracheotomy. Schafer also prevented it by dividing the thyreo-arytenoid ligaments by means of an electro-cautery passed down through the animal's mouth. A division of the pneumogastric on each side, below the separation of the recurrent laryngeal nerves, is not followed by the change in the breathing which follows the division of the nerves higher up. Apart from asphyxia, the death which follows double vagotomy is principally due to congestion of the lungs. Instead of alternate afferent and inspiratory and expiratory impulses regulating respiration passing up through the vagi, impulses may originate and travel to the respiratory centre in other ways, e. g. from the muscles of respiration and the diaphragm through the spinal cord.

Porter and Newburgh's experiments tend to show that the rate of respiration is excited by centripetal impulses through the vagus from the lungs, the ends of the vagus being stimulated by the excess of CO_2 in the circulating blood. They experimented on dogs in which pneumonia was set up artificially. The right vagus was divided in the chest below the separation of the right recurrent, and, after this wound had healed, then the left vagus was divided in the neck. Thus the asphyxial complications following the usual double vagotomy were avoided. If, after this vagotomy, pneumonia was set up in the dog, the rate of respiration remained normal and the respiratory centre did not become exhausted.

The immediate effect of injury to the vagus in the neck, viz. the arrest of respiration, may be regarded as due to an afferent current of injury. In the same way a foreign body lodged in contact with the nerve may keep up a continued afferent impulse of irritation. When there is paralysis of the soft palate and pharynx, the larynx is irritated during swallowing, so that a cough is occasioned. If the superior laryngeal is also paralysed food enters the trachea and then there is further irritation.

The afferent fibres which, when stimulated, cause a reflex vasodilatation with slowing of the heart, and which correspond with the depressor nerve in the rabbit, leave the trunk of the vagus with or just below the superior laryngeal to join the superior cardiac nerve of the sympathetic. The fibres may run in the external laryngeal branch after its separation from the internal laryngeal.

Numerous instances of collapse and sudden death have been attributed to the stimulation of the superior laryngeal or the external laryngeal branch during an operation. The inclusion of the vagus in a ligature is for this reason dangerous, whereas the division of one vagus has little effect on the heart or respiration. Thus Weber reported that in removing a tumour from the neck the vagus was included in a ligature, and the patient died half an hour later in collapse.

The cervical sympathetic. The dilator fibres of the pupil are derived from the 1st, 2nd, and 3rd thoracic nerves, some say also from the 7th and 8th cervical. The motor fibres to the involuntary muscle of the orbit and the non-striped fibres of the levator palpebrae arise higher up, viz. from the 1st to the 4th or 5th cervical nerves. Both these sets of motor fibres pass to the ascending branch of the superior cervical ganglion; then, by way of the carotid artery and Gasserian ganglion, along the first division of the 5th nerve and its long ciliary branches, to the eye. The vasoconstrictor fibres are derived in the dog from the 2nd, 3rd, and 4th thoracic, in the rabbit from the 2nd–8th thoracic nerves. The origin of vasodilator fibres is still uncertain. Secretory salivary gland fibres and probably secretory sweat gland fibres to the head, neck, and upper limb come from the 2nd and 3rd thoracic; pilomotor fibres to the face and neck of the monkey from the 2nd to the 5th thoracic. The accelerator fibres of the heart are derived between the 1st and 5th, but especially from the 2nd and 3rd thoracic.

After the divison of the vagosympathetic in the neck of dogs and cats Schafer found that the signs of sympathetic paralysis persisted for more than two years, although somewhat less marked than at first. There was still dilatation of the vessels of the ear, lachrymation, and salivation, a contracted pupil, a sunken eyeball. If after the lapse of this period the sympathetic was divided on the opposite side, the paralytic effect was marked. Then on the side first divided there was a reversal from the previous signs of paralysis to those of slight excitation, partly to be explained by regeneration from the spinal cord.

Afferent vasomotor fibres of the upper cervical sympathetic are distributed with the peripheral fibres of the facial. The deep petrosal nerve passes from the plexus on the internal carotid artery to the pterygoid canal, where it is joined by the large superficial petrosal from the geniculate ganglion of the facial to form the vidian nerve which is continued to the sphenopalatine ganglion. From the ganglion fibres are distributed to the nasal fossae and sinuses and to the palate.

Mirallié and Émile-Weil showed that this connexion between the cervical sympathetic and the facial might be used to distinguish a central from a peripheral lesion. Stimulation by a pledget of cotton-wool of the nasal mucous membrane near the anterior and posterior nasal orifices caused a congestion of the face and a secretion of tears. This reaction is lost in the case of peripheral facial paralysis, recent or of old standing, but persists unaltered in central facial paralysis. Inhalation of nitrite of amyl causes congestion of the side of the peripheral facial paralysis, the same as on the sound side.

Laignel-Lavastine and Courbon reported that a soldier was wounded by a German rifle bullet, which entered at the anterior border of the right sternomastoid muscle on a level with the thyroid cartilage, and, after taking a vertical course, was found by the X-rays lodged to the right side of the 2nd dorsal vertebra, its nose being 1 cm. from the upper border of the 3rd vertebra. The man lost much blood at the time, which rendered him anaemic for a month; also he lost his voice, which was diagnosed as hysterical aphonia. 3½ months later the man presented the characteristic signs of injury to the right cervical sympathetic, slightly modified because he had always had prominent eyeballs. There was a contracted right pupil and a narrowing of the palpebral fissure, but without any tendency to ptosis. There was a diminution of sweating in the right cervico-facial region extending to the level of the spine of the 7th cervical vertebra, including the deltoid region and the line of the 2nd rib. There were no vasomotor troubles; the tension of the eyeballs was normal, also the light and accommodation reflexes. The cilio-spinal reflex could be obtained; when the skin of the right side of the neck was pinched the right pupil dilated slightly. On compressing the right eyeball the heart-beats diminished by 16, as compared with a diminution by 12 beats on the left. This indicated that the vagus influence was less opposed by sympathetic acceleration on the right side than on the left. The bullet had injured in particular the ramus communicans after it had separated from the 1st thoracic root immediately outside the intervertebral foramen.

Ridder referred to nine cases of injury to the cervical sympathetic in the neck previously reported by Gross, and he added a tenth. A pioneer, aged 23, was wounded by splinters of a shell in several places, including one which entered under the left ear, and which was extracted. Five months later there was a scar with deep connexions at the above spot. The left side of the face was redder and slightly flattened by wasting; the left pupil was contracted, the palpebral fissure smaller, the eyeball sunken. The reaction of the pupil to light and accommodation was normal and there was no noteworthy disturbance of salivary secretion or sweating.

The abducent or 6th nerve and the syndrome of Gradenigo. The 6th nerve may be disturbed at four points in its course: (1) After it has emerged from the lower edge of the pons it runs for 15 mm. in the subarachnoid space between the pons above and the occipital bone below. It is here liable to become involved in meningitis, including the toxic effect of injections to produce spinal anaesthesia. (2) The nerve next enters an aperture in the dura mater to the inner side and slightly below the 5th nerve, it passes to the outer side of the petrosal sinus and crosses over the apex of the petrous bone beneath the petrosal sinus and the sphenoidal ligament. This course through rigid structures renders it liable to be involved in fracture of the base of the skull, also in operations for the complete removal of the Gasserian ganglion or the division of the main root of the 5th nerve. The syndrome noted by Gradenigo is that in which diplopia from paralysis of the external rectus follows on suppuration in the middle ear. In Torrini's case acute mastoid suppuration and lateral sinus thrombosis was followed by diplopia, owing to paralysis of the external rectus on the same side. Dutheillet de Lamothe also described similar associations, and added an exceptional instance in which the paralysis was on the opposite side to the otitis. This exception may have been the result of an extension across by way of a venous sinus, or due to compression by the suppuration on the diseased side displacing the pons. Bellin, Aloin, and Vernet described a case in which the 6th nerve was involved along with the 4th, 5th, and 7th nerves. A carbuncle on the neck was followed by diplococcal meningitis and septic thrombosis of venous sinuses within the skull. There were found collections of pus in the region of the foramen rotundum, the foramen ovale, and the parotid region. (3) The nerve then enters the cavernous sinus and passes forward along the outer side of the carotid artery to reach the outer wall of the sinus. A lesion limited to the nerve at this stage of its course was described by Spencer. A soldier, after a kick by a horse upon the temple, developed a cavernous varix, i. e. a small communication between the carotid and cavernous sinus. There was an absence of signs of fracture of the base, of an aneurysmal sac, and indeed of any other lesion except permanent paralysis of the external rectus. (4) Beyond the cavernous sinus. Balla's patient, a prisoner of war, was attacked by acute suppurative otitis, followed by suppuration under the temporal muscle, which was incised five weeks after the commencement of the otitis. A paralysis of the 6th nerve on the same side was noted; 3½ weeks later, i. e. on the 54th day of the illness, the mastoid antrum was opened, and this exposed extensive suppurative osteomyelitis. The abducent paralysis passed off at the end of three months.

The syndrome of Hughlings Jackson. Hughlings Jackson, in 1864, in a lecture 'On the Study of Diseases of the Nervous System', included the following case among instances of hemiplegia from diseases of the same sort, but at different points in the motor tract: '4, sudden and complete paralysis of the tongue, palate, and of the vocal cords (*sic*), all on the left side; weakness of the left limbs and slightly of the right. Clot involving the lingual and spinal accessory nuclei, and implicating the fibres from (*sic*) the limb, about their decussation' . . . 'This is physiological evidence that he has disease, as Lockhart Clarke's researches clearly show, at the nucleus of the lingual and spinal accessory nerves.'

After the first case Hughlings Jackson described others of a similar kind, and some writers refer, under the term 'syndrome of Hughlings Jackson', to cases still obscure as to causation. Thus Arrowsmith described the clinical symptoms and the results of the post-mortem examination in a man aged 54 who had begun to suffer a year before from indistinctness of speech and slight difficulty in swallowing. The Wassermann test gave a negative result. The symptoms progressed until speech was hardly intelligible; in attempting to swallow, a bolus of food was expelled from the mouth by the forcible contraction of the pharynx, after the impairment of the contractility of the fauces. Once in the oesophagus the bolus passed down. He could not whistle; movements of the tongue were slow and uncertain. There was a steady progress of the paralysis until the patient's death, when there was found degeneration and atrophy of the motor nuclei of the 5th, facial, glossopharyngeal, pneumogastric, bulbar, and spinal roots of the accessory. No cause could be assigned, and Arrowsmith had seen three other cases, all in males beyond middle life. The disease might terminate suddenly by bilateral laryngeal abductor paralysis unless tracheotomy were done in time, or the fatal result might be determined by a further paralysis of the oesophagus.

Körner noted the case of an officer, aged 20, who was struck by a bullet on the occipital bone 3·5 cm. to the right of the occipital protuberance, and 1 cm. above the superior curved line. Later there was a scar at the spot 1 cm. in diameter. The bullet must have passed through the back of the right occipital lobe near the right lateral sinus, through the lateral lobe of the cerebellum, across the right cerebellar fossa, and then have penetrated the base of the skull towards the apex of the petrous portion, having the margin of the basilar process on the inner side, the jugular foramen, the internal auditory meatus, and the carotid canal to the outer side. The base of the bullet stuck in the skull, and its point was felt in the soft tissue of the wall of the nasopharynx near the orifice of the right Eustachian tube. On hooking forward the palate, the point of the bullet was seen to cause a prominence of the mucous membrane. The patient did not lose consciousness, but had to be carried to the ambulance, the voice was hoarse, there was a difficulty in speaking, swallowing was difficult and painful, there was repeated spontaneous vomiting, also pain in the head and giddiness when attempting to stand. But no bleeding occurred from the mouth, nose, or throat. When examined 26 days after the injury, it was found that the pupils, eye-muscles, the facial and 5th nerves were uninjured, also the sternomastoid and trapezius. There was paralysis of the right half of the tongue, of the soft palate, pharynx, and vocal cord, and a corresponding loss of sensation. The sense of taste to quinine was diminished on the right side. On applying citric acid there was a marked flow of saliva from the left parotid, but not from the right. There was complete deafness in the right ear and an absence of the vestibular reactions which could be obtained on the left side. When the eyes were shut there was no giddiness; the patient could walk with closed eyes, but deviated to the left; he could stand and turn round all right with closed eyes. He had full muscular control; there were no abnormal reflexes or muscular movements of the limbs. The temperature remained normal; the pulse, after the accident, was increased to 108, but later was between 80 and 90.

In this case the bullet appears not to have injured any nuclei within the brain, but only nerve-roots, either in their intracranial course or within the foramina. As the cochlear and vestibular portions of the auditory nerve were injured whilst the facial escaped, it was concluded that this must have been due to haemorrhage. The same explanation may be applied to the paralysis of the glossopharyngeal, pneumogastric, and bulbar roots of the accessory. The hypoglossal nerve was outside the track of the bullet; but it may have been injured by a fissured fracture of the occipital bone. It is remarkable that whilst the hypoglossal was injured, also the bulbar roots of the accessory, the spinal roots supplying the sternomastoid and trapezius escaped. The lateral and petrosal sinuses could not have been extensively involved, for there was an absence of signs of wide basal haemorrhage.

Cases of paralysis of the pharynx, larynx, and shoulder have been noted as a result of fracture through the base of the skull. Lüken referred to 12 cases which had been previously published and added a 13th, in which, after a fall on the head, the auditory, pneumogastric, and accessory were involved, whilst the facial, glossopharyngeal, and hypoglossal were uninjured. Following upon the injury there was deafness, also loss of vestibular reactions, paralysis of the soft palate, pharynx, larynx, and oesophagus on the side of the injury, but sensation was retained, also the sternomastoid and trapezius were paralysed. By means of the X-rays a fissured fracture was traced running from the foramen magnum, through the jugular foramen and carotid canal, to the cribriform plate. There were at first disturbances of the heart and respiration, but these could not be clearly distinguished from the symptoms of concussion. After 7½ months there was partial recovery, and after a year complete recovery, of the soft palate, pharynx, sternomastoid, and trapezius, but there persisted a paralysis of the laryngeal and oesophageal nerves.

Lesions of the nerves at their exit from the skull. The so-called syndrome of the foramen lacerum posterius appears to have been described by Stephen Mackenzie in 1883, and in a further note in 1886. Syphilitic disease had caused paralysis of the soft palate, tongue, and vocal cord, also of the trapezius and sternomastoid muscles, all on the same side. There was also on the left side a contracted pupil, a recession of the globe, and a narrowed palpebral fissure. There was no paralysis of the limbs, nor of the facial or 5th nerves. The condition persisted for four years, during which the only development was an enlargement of glands in the neck, which subsided under the administration of iodide of potassium. Then there appeared a paralysis of the left teres minor which indicated a further spread of the disease.

The name 'syndrome of the foramen lacerum posterius' was applied by Vernet in 1916, and he added, in 1917, a description of the case of a man aged 52, suffering from syphilis, in whom enlargement of lymphatic glands caused pressure on the nerves at their exit from the foramen. The enlargement followed upon a chancre of the lip, and subsequent to the swelling of the glands on the right side the man suffered from loss of voice, difficulty in swallowing solids, cough, and an excessive formation of saliva and mucus. There was no paralysis of the tongue, the soft palate was paralysed so that the uvula appeared deviated to the left, and in phonation the palate was drawn upwards and to the left. This happened also during swallowing, when fluids escaped by the nose. The voice had a nasal twang, with hoarseness, due to paralysis of the vocal cord, which was stationary in the cadaveric position. There was a diminution of sensation on the right side of the soft palate, pharynx, and larynx, which gave rise to a choking sensation. Sensation in the auricular branch of the vagus was normal, indicating that the lesion was below its origin, also sensation was unimpaired in the hard palate supplied by the 5th nerve. Taste was diminished to quinine on the back of the right side of the tongue. The pulse-rate was 100. The facial, auditory, and the spinal accessory nerve to the sternomastoid and trapezius were unchanged. All these symptoms rapidly subsided simultaneously with the glandular swelling under [antisyphilitic treatment.

As to a *combined posterior lacerate or jugular and condyloid foramens syndrome.* Sicard and Rimbaud distinguished two types, endocranial and exocranial, of paralysis of the glossopharyngeal, pneumogastric, accessory, and hypoglossal nerves. In the endocranial type there was in addition loss of taste; in the exocranial form the innervation of taste was not disturbed. In the endocranial case which they described, a syphilitic meningitis had involved the last four cranial nerves in their course between the brain and the dura mater, and in addition caused excitation of the pyramidal tracts immediately close to their crossing. In the exocranial lesion, when the nerve of Jacobson escapes injury, the sense of taste is not disturbed.

Rimbaud and Vernet saw another case of this combined syndrome. A man was wounded in the right temporo-maxillary region just below the ear at the point of exit of the facial nerve. The lower division of the facial was the more severely injured, the upper to a less extent. This was combined with partial injury to the glossopharyngeal, pneumogastric, bulbar roots of the accessory and hypoglossal. There was impairment of taste: quinine was perceived imperfectly on the posterior third of the tongue. There was a spasmodic cough, salivation, and hyperaesthesia of the soft palate, pain in the throat of that side, with shortness of breath. There was paralysis of the soft palate and superior constrictor; the uvula was deviated to the opposite side, and food passed into the nose. The voice was thick, with the right vocal cord in the cadaveric position. The pulse was irregular, with transitory tachycardia. There was paralysis of the right half of the tongue, but the sternomastoid and trapezius were normal. The foreign body was removed from behind the angle of the jaw.

The case recorded by Gross was an illustration of persistent irritation of the pneumogastric by a foreign body lodged a little below the foramen lacerum posterius. An officer was wounded by a fragment of shell which entered through the anterior border of the middle of the left sternomastoid. The immediate effect was loss of voice with external haemorrhage, so that he fainted. On his recovery from the faint he had respiratory spasm and a feeling of suffocation, so that the question of tracheotomy was raised. The feeling of want of air diminished, but an irritating cough persisted. On examination a paralysis of the left side of the palate and of the left vocal cord was found. The left side of the palate, pharynx, and larynx were anaesthetic, and there was also paralysis of the left half of the tongue and loss of taste. The sternomastoid and trapezius had escaped. The foreign body, a fragment of shell, was seen by the X-rays below the foramen, and an exploration in order to remove it was attempted a month after the injury. However, the vertebral artery was wounded, and the operation abandoned. After the exploration he had attacks of collapse with cold sweats, superficial respiration, the pulse slowed to 54, followed by recovery after four hours. It was discovered that these attacks were brought on by over-eating in the presence of an irritable vagus. When over-eating at any one meal was stopped, the attacks ceased.

The syndrome of the retroparotid space. Villaret and Faure-Beaulieu began by naming four syndromes already recognized.

(1) The syndrome of Avellis, hemiparesis of the soft palate and larynx.

(2) The syndrome of Schmidt, the hemiparesis of the soft palate, larynx, sternomastoid, and trapezius.

(3) The syndrome of Hughlings Jackson, the hemiparesis of the soft palate, larynx, sternomastoid, and trapezius, together with hemiparesis of the tongue.

(4) The syndrome of Tapia, the hemiparesis of the larynx and of the tongue, with or without paralysis of the sternomastoid and trapezius, the soft palate remaining active because the lesion to the vagus was below the separation of the nerves to the palate. Tapia noted this injury as having been inflicted on toreadors by the bull's horn.

The syndrome of the retroparotid space consists in the hemiparesis of the glossopharyngeal, the pneumogastric, the accessory, the hypoglossal, and the cervical sympathetic. The retroparotid space is bounded behind by the cervical column, within by the pharynx, externally by the sternomastoid, in front by the parotid, above by the base of the skull with the foramen lacerum posterius. It contains the internal carotid and jugular vein, with the 9th, 10th, 11th nerves, and the 12th before it takes on its horizontal course, also behind all the sympathetic. The distinguishing feature of this syndrome is the involvement, with the other nerves, of the cervical sympathetic. One of the cases may be noted because the simultaneous injury to the internal carotid necessitated a ligature of that vessel which caused some cerebral anaemia. A soldier was wounded by a fragment of shell which entered 1 cm. behind the angle of the mandible on the right side; he was able to call out loud for help three times and then lost his voice. In a few minutes a large haematoma formed in the right side of his neck and caused a feeling of suffocation. He had pressed on the wound, and his breathing became freer when the pressure was removed and there was a free escape of blood. Two days later the right internal carotid was found divided 3 cm. above its origin and a ligature was applied to each end. From that time his symptoms had persisted until examined four months after being wounded. He then presented signs of paralysis of the right cervical sympathetic, a smaller palpebral fissure, a sunken globe, the pupil contracted but with the reflexes normal; he was hoarse from paralysis of the right vocal cord, and had difficulty in speech from paralysis of the right half of the tongue; he had trouble in swallowing, not due to the soft palate, which was not paralysed, but to the pharynx. There was a partial loss of taste towards the back of the tongue on the paralysed side. Moreover, there were signs of partial cerebral anaemia, right hemicrania, giddiness and nausea following fatigue, and some loss of memory.

In two of the four cases referred to the position of the foreign body as localized by the X-rays corresponded with the clinical observations.

Vidoni described a case resembling those noted by Villaret and Faure-Beaulieu. A soldier received a bullet in the nape of the neck to the right of the middle line, which lodged in the right maxilla. He was under observation for the following month. The injury set up respiratory and cardiac disturbance, inequality of the pupils, paralysis of the tongue and of the soft palate on one side. There was a curtain movement of the posterior wall of the pharynx from right to left, and extreme difficulty in swallowing.

Beck described another instance of the syndrome of the retroparotid space. A man had been stabbed in the neck by a knife, and blood escaped from the nose and mouth, as well as from the wound. He fell to the ground and lost consciousness for a time; bleeding from the wound soon stopped, but continued for a while from the nose and mouth. The wound healed, and five months later he was hoarse, had difficulty in swallowing, got easily out of breath, and was subject to giddiness and headache. There was found a scar 1·5 cm. in length and four fingers broad behind the right ear. The right vocal cord was paralysed, the right pupil contracted; there was slight ptosis of the right upper eyelid. There was diminished sensitiveness of the right side of the head supplied by cervical nerves. There was right facial paralysis, also of the right hypoglossal with loss of taste on that side. The sternomastoid and trapezius were not paralysed.

Paralysis of the 7th to the 12th cranial nerves, together with the cervical sympathetic. D'Oelsnitz and Cornil examined a sergeant aged 36; a fragment of shell had penetrated his right external auditory meatus; it had divided the facial nerve near its exit from the Fallopian canal; it caused a partial injury to the cochlear and vestibular nerves; it had then crossed the back of the parotid region, fractured the palatal process of the right maxilla, and was found lodged behind the left angle of the jaw. There was no injury to the large blood-vessels. Tracheotomy had to be performed because asphyxia threatened, but the tube was removed two days later.

The patient presented facial paralysis of the peripheral type, paralysis of the right sympathetic, the pupil contracted and the eyeball retracted with diminished tension. There was diminished hearing; impaired vestibular reactions, and loss of the oculo-cardiac reflex. There was paralysis of the soft palate and pharynx of the right side with disturbance of deglutition; the right vocal cord was stationary in the cadaveric position. The right sternomastoid and the upper part to the trapezius were paralysed, also the right half of the tongue with diminution of taste towards the back of the tongue on that side. The case thus presented an association of the symptoms following injury to the middle ear combined with the syndrome of the retroparotid space, four cases of which were described by Villaret and Faure-Beaulieu.

A subparotid syndrome. Moreau described an injury which differed from the syndrome of the foramen lacerum posterius. The glossopharyngeal and the hypoglossal nerves escaped because the bullet had passed under their respective loops; it also passed behind the spinal accessory nerve. The vagus and the sympathetic were paralysed and there was partial paralysis of the peripheral fibres of the 5th and 7th nerves on the face.

A soldier was struck by a bullet below the horizontal ramus of the mandible on the left side, about 3 fingers' breadth in front of the angle, and it made exit at the nape of the neck to the left of the middle line. This caused immediately dysphonia and a sense of suffocation. The wound healed, and two months later the man presented a left sunken eye, a narrowing of the palpebral fissure, and a contracted pupil. The pupil reacted to light and accommodation, the tension of the eyeball was normal and the vision good. There was paresis of the left facial as shown by an incomplete closure of the eyelids and an obliquity of the labial fissure, along with a slight diminution in sensation. There was paralysis of the left side of the soft palate with a deviation of the uvula to the right, also attacks of cough and dyspnoea on walking fast. The glossopharyngeal had escaped injury, and the sternomastoid and trapezius were not paralysed.

Sicard, Roger, and Vernet noted a lesion between those causing the retroparotid and the subparotid syndrome respectively. A surgeon attempted to cure an obstinate case of neuralgia of the ear and pharynx, in type apparently resembling trigeminal neuralgia. He aimed at excising the sympathetic together with the pharyngeal branches of the glossopharyngeal and vagus. He did this without setting up laryngeal paralysis or respiratory or cardiac disturbance, but the hypoglossal and the spinal accessory nerves were divided, in addition to the glossopharyngeal and the auricular and pharyngeal branches of the vagus.

Körner records a case of complicated injury of nerves. A grenadier aged 23 received a bullet which entered over the right zygoma, 3 cm. below the right external canthus and lodged beneath the skin midway behind the posterior border of the sternomastoid and the line of the spinous processes, half-way between the base of the skull and the shoulder. The bullet smashed the zygoma and caused a fracture of the anterior cerebral fossa. The resulting haemorrhage produced double optic neuritis and paralysis of the external rectus. This impaired vision and set up diplopia. Also the coronoid process of the mandible was fractured on the right side, rendering the movements of the jaw stiff. There were signs of paralysis of the 10th, 11th, and 12th nerves. There was no bleeding from the mouth or ear and no dyspnoea. 55 days after the injury there persisted weakness of the external rectus, double optic neuritis, the mouth could only be opened 2 cm., the right half of the tongue, soft palate, and the right vocal cord remained paralysed, and the right arm could only be raised to the horizontal, owing to the paralysis and atrophy of the sternomastoid and trapezius. Here, as the mouth could not be opened, it was impossible to decide as to the injury to the glossopharyngeus. It was also uncertain whether the spinal accessory was struck where it was in connexion with the vagus, or lower down.

3½ months after the injury an incision was made along the anterior border of the sternomastoid and, after removing enlarged lymphatic glands and scar tissue, the vagus, hypoglossal, and spinal accessory nerves were found to have been compressed but not actually injured. Six weeks after this neurolysis partial recovery in the tongue, sternomastoid, and trapezius was noted, but not of the paralysis of the soft palate and vocal cord. Meanwhile the paralysis of the external rectus and the optic neuritis had disappeared.

The recurrent laryngeal nerves. Gütt collected 154 cases of paralysis of the recurrent nerves from Gerber's Klinik. 19 were distinguished as of central origin, of which 6 were due to tabes and 13 were combined with paralysis of the 9th to the 12th cranial nerves. Of these latter, 3 were attributable to influenza, 3 to syphilis, 1 was a case of progressive bulbar paralysis, 2 syringomyelia, in 1 an injury had caused haemorrhage into the nuclei of the 7th to the 11th nerves, in 3 there was a combined paralysis of the larynx, sternomastoid, and trapezius. Among the cases of peripheral pressure paralysis were:

19 by aneurysms.
10 by bronchoceles, 9 on the left side.
7 by cardiac dilatation, either the left auricle or the aortic arch.
19 by cancer of the oesophagus.
8 by tumours in the neck.
1 by an enlarged thymus.
1 by enlarged mediastinal glands.
2 by mediastinal tumours.
7 by disease of the pulmonary apex, 6 on the left side.
6 due to neuritis, toxic, diphtheritic, alcoholic, syphilitic, influenzal.

There are rare cases such as those mentioned by von Schrötter at the German Medical Congress in 1901. In one case the left recurrent laryngeal nerve was compressed between a dilated ductus Botalli and the aorta, and in another between the left pulmonary artery and the ligamentum arteriosum; in both there was mitral stenosis.

The left vagus, including the recurrent, was injured deep in the neck, together with the left phrenic nerve, in a case described by Gutzmann. A splinter of shell had entered under the crest of the left scapula and was found by the X-rays and removed from the left sternoclavicular articulation. It had produced paralysis of the left vocal cord with hoarseness, difficulty in swallowing, and dyspnoea from paralysis of the left half of the diaphragm. The pulse was variable—at times 40–50, then suddenly rising to 130 a minute. When speaking and swallowing, the head was bent to the left as if by an overaction of the sternomastoid and trapezius. There was therefore evidence of disturbance of cardio-inhibitory and cardiac accelerator mechanisms; paralysis of the fibres derived from the bulbar roots of the accessory, and overaction passing through its spinal roots.

A case described by Körner. A fusilier aged 22 was wounded by a bullet which entered at the anterior border of the left sternocleidomastoid midway between the mastoid process and the clavicle at the level of the upper border of the thyroid cartilage and 1·5 cm. behind the posterior margin. The bullet lodged under the skin of the posterior border, 2 cm. below the spine of the left scapula. This caused paralysis of the left soft palate, vocal cord, and brachial plexus, but the sternomastoid and the trapezius remained active, there was no dyspnoea and no spitting of blood. 76 days later there persisted a paralysis of the left recurrent from which it was concluded that the left vagus must have been involved in haemorrhage or just grazed, for there was no injury to blood-vessels.

There appears to be no case on record of recovery after complete division of the recurrent laryngeal nerve. Shelton Horsley reunited the left recurrent laryngeal nerve which had been partially divided by a pistol bullet 3 months before in a woman aged 40. The nerve, behind the left lateral lobe of the thyroid gland, just before it enters the larynx, was found to be involved in a mass of scar tissue. The nerve had not been completely divided; the scar tissue was excised and sutures applied. 16 months later the left vocal cord had almost recovered its motility: it only lagged a little behind the right, and the voice had lost its hoarseness.

The following case appeared at first to be one of injury by a bullet to the laryngeal and oesophageal branches of the right pneumogastric. Subsequently the early and stationary characteristics of the lesion seemed to change as if the bullet had induced an inflammatory extension to the spine. In the end it was found out that the man had been suffering from cancer of the oesophagus, which had spread and caused paraplegia by compression of the spinal cord. The cancer was situated close to the site of the bullet, but there was a small interval of normal tissue between. The cancer was of the common kind and there is no necessity for assuming that it was a sequela of the gunshot injury. Indeed, it is much more likely that the disease was established before the injury. The complex nature of the case was cleared up by the aid of G. J. Randall, F.R.C.S., the Resident Surgical Officer at the 4th London General Hospital.

A sergeant aged 37 was wounded at Ypres on April 24, 1917. A shrapnel ball penetrated his face, carried away teeth from the right upper jaw, wounded the palate on the right side, and lodged in contact with the outer surface of the right ala of the thyroid cartilage. It could be felt in this position as a small hard body and was identified in this position by the X-rays. After recovery from the general effect of the injury, he continued hoarse and had some difficulty in swallowing, so that he had, as he said, to make 'two or three swallows' when at a meal of meat and potatoes. After a time in hospitals in France and in this country, he went on furlough on June 29. Then there arose pain in the neck and back which became defined as girdle pain at the level of the 2nd and 5th dorsal nerves, also rapidly increasing weakness of the arms and legs set in just before his admission to the 4th London General Hospital on August 6. There he was examined by Captain Tunnicliffe, who found that the man was suffering from pressure paraplegia at the level of the 2nd and 3rd dorsal nerves. There was an angular projection of the 2nd and 3rd dorsal spines and an X-ray examination showed erosion of the anterior surfaces of these vertebrae. The hoarseness was seen to be caused by paralysis of the right vocal cord, which was stationary in the cadaveric position. There was difficulty in swallowing, but without pain; there was a persistent dry cough without expectoration.

The paraplegia became complete with paralysis of the bladder and rectum and the formation of a sacral bed-sore. Consequently, the man came under the care of the reviewer and on August 31 the spinal cord was exposed by laminectomy. The cord and theca were intact, and after the removal of laminae it pulsated well. There was extensive softening of the 3rd and 4th thoracic vertebrae, and erosion, so that the two bodies moved on one another; the soft tissues around were very vascular and infiltrated by new growths. There was an absence of all signs of pus. The patient was not made worse by the operation, but there was no improvement and he died on September 20, 5 months after being wounded and about 2 months after the commencement of pressure on the spinal cord.

At the post-mortem the shrapnel bullet was found surrounded by fibrous tissue in relation with the outer surface of the right ala of the thyroid cartilage, just above the limit of the new growth. The right vagus and superior laryngeal nerve were involved in scar tissue after partial division by the bullet. A cylindrical mass replaced the oesophagus for 1½ inch, with a channel through it corresponding in dimensions with the lumen of the trachea, having the structure of squamous-celled carcinoma. The growth had spread and infiltrated the 3rd and 4th dorsal vertebrae, also the lower cervical and mediastinal lymphatic glands. In the liver there were several metastatic growths, the largest of the size of a small potato.

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W. G. S.

THE CLINICAL VARIETIES OF LETHARGIC ENCEPHALITIS AND THEIR CLASSIFICATION

The original clinical picture by which lethargic encephalitis was first recognized in this country in 1918 has given place to a multitude of clinical 'types'. Many of these at first sight appear to have little or nothing in common and are only grouped with the well recognized syndromes because in certain instances they have formed a phase in the clinical course of an undoubted case of lethargic encephalitis. Thus cases indistinguishable from chorea gravidarum (Carnot and Gardin, Lereboullet and Mouzon, Lesné and Langle), cases of simple attacks of hiccough (Dufour), and others presenting a pure picture of spinal radiculitis are alike being diagnosed, more particularly in France, as conditions due to the virus of lethargic encephalitis.

It is of course to be expected, as Buzzard and Greenfield have pointed out, that an inflammatory disease of the nervous system should give rise to a versatile symptomatology: the structure of this system is so complex and the functions of its several parts so highly specialized. Further, Netter has called attention to the fact that a given virus may vary in its action, at one time producing convulsions, at another paralyses, as lead, alcohol, and the virus of rabies have long been known to do. Moreover, in successive epidemics of any infective disease there may be remarkable clinical variations in the course and form of the malady. In all probability, therefore, there are numerous factors underlying the protean manifestations of lethargic encephalitis, and of these a change in the localization of the virus in the nervous system (Ellis) is but one, and probably not the most important.

Motor manifestations of various kinds, ranging from the intense psychomotor excitement of some delirious cases to choreiform movements, tremor, and clonic twitchings of isolated muscles or parts of muscles have been reported by various observers since the first appearance of the disease, but they have undoubtedly become more frequent of late and in many recently recorded cases have quite dominated the clinical picture. Clearly their occurrence must increase still further the number of possible combinations of symptoms—that is, of symptom-complexes—that we may expect to encounter; indeed the number already recorded is rapidly growing. In consequence, a comprehensive view of the essential features of the disease becomes increasingly difficult. Confusion has been worse confounded by the many, and for the most part inadequate, attempts to divide the disease into clinical 'types'. The bases of classification adopted by different writers are as diverse as they are numerous. In many of them the presence of some prominent symptom—general or nervous—in a series of cases is made the basis for the definition of a 'type', and sometimes even a single example of some striking syndrome is so labelled, with the result that now every case of lethargic encephalitis falls into almost as many 'types' as it has symptoms, either simultaneously or successively.

The recently named 'myoclonic types' (Sicard and Kudelski) affords a striking example of this. Sicard's original series consisted of four cases characterized by an onset with slight fever and intense neuralgic pains. In a week or so there appeared rhythmical clonic contractions of various muscles in head, trunk, and limbs. There was neither lethargy nor palsies of cranial nerves, and when the disease was fully established there was insomnia with delirium, increasing restlessness, hallucinations, and finally general psychomotor excitement. Coma and death completed the picture. At first sight it seems justifiable to class together as a type cases showing a symptom-complex so clear-cut and so striking. However, further experience indicates that not only are pure cases extremely rare, but that in most instances all these symptoms are either superimposed upon, precede, follow, or alternate with one or other of the numerous symptom-complexes of the disease. Further, single elements of Sicard's 'acute myoclonic encephalitis' may occur as isolated symptoms in cases of every clinical variety of lethargic encephalitis. Hence we find classed as 'myoclonic' cases varying clinically in the widest possible manner, and frequently having nothing in common but some clonic twitchings of one or more isolated muscles, or parts of muscles.

Moreover, the term myoclonus is being applied to such a variety of involuntary muscular movements and contractions that it has quite lost its original meaning. When we find Bourges and Marcandier describing a 'forme mixte à symptoms intriqués (co-existence de somnolence, paralysies partielles oculaires, mouvements choréo-athétosiques, secousses myocloniques, catatonie et troubles delirants)', and Kahn reporting 'Un cas d'encéphalite successivement névralgique, psychique, choréiforme, myoclonique, léthargique avec sequelles hémi-myocloniques après la guerison', it becomes clear that a disease of this character defies a purely symptomatic classification.

Probably no perfect classification of the forms of the malady is yet possible, yet it is reasonable to suppose that an analysis of the symptoms might reveal certain general principles upon which some uniform and single basis of classification could be founded.

The symptoms of such infective diseases of the nervous system as acute poliomyelitis (Heine-Medin) or lethargic encephalitis fall naturally into the following groups:

- *General Symptoms*—Signs of toxi-infection . . . . fever, shivering, cutaneous eruptions, pains and malaise, gastro-intestinal disorders such as vomiting, constipation, foul tongue, &c.
- *Nervous Symptoms* . . .
  - general . .
    - 'positive' . . . delirium, mania, restlessness, hallucinations.
    - 'negative' . . lethargy, coma.
  - localizing .
    - 'positive' . . convulsions, involuntary movements and muscular contractions, rigidity, ataxy, pain.
    - 'negative' . . paralyses.

The terms 'positive' and 'negative' are employed in the sense in which Hughlings Jackson originally used them; positive symptoms being the expression of exalted function, either from irritation or from loss of higher control, and negative symptoms expressing loss or depression of function from destruction of nervous structures or otherwise. The recognition of these two classes of symptoms is extremely helpful in the consideration of lethargic encephalitis, as in that of every other nervous disease. We are enabled to localize positive symptoms that would otherwise be obscure, and to understand that a lesion of a single area may give rise to a convulsion as well as to paralysis, and that whether a clonic twitching of a muscle or weakness of it occurs does not depend necessarily upon the site of the lesion but upon its nature.

In practically every case of lethargic encephalitis there are focal, or localizing, nervous symptoms, and although these do not represent the full extent of the involvement of the nervous system, yet they do indicate the topography of a known lesion. In any series of cases taken at random, the presence of such focal symptoms is the only common factor. Beyond the general statement that a case with pronounced positive motor symptoms is likely to show other positive symptoms, such as pain, delirium, or hallucinations, we can only regard the combination of symptoms in a given symptom-complex as fortuitous and subject to no laws that we know of. If this be the case, it seems probable that a **classification upon an anatomical basis**, like that adopted for acute poliomyelitis, is the only remedy for the confusion that characterizes written accounts of lethargic encephalitis.

Even this cannot be entirely satisfactory. Acute poliomyelitis is a much less polymorphic disease than lethargic encephalitis, yet Wickmann found it necessary to add a clinical type (the abortive type) to his anatomical types. Nevertheless, the adoption of an anatomical classification based upon the topography of the focal nervous symptoms would make it impossible for a single case to belong to six or eight so-called types, and would ensure a common terminology in descriptions of the disease.

In the absence of any bacteriological or serological standards it is not always possible to know whether a given symptom-complex should be included in the rapidly growing group attributed to this disease or not.

A study of the recorded cases makes it seem highly probable that from time to time cases are incorrectly included. Some of the choreiform cases of the French writers seem particularly open to question in this respect. Therefore, any scheme of classification must at present be cumbered with cases of doubtful origin. Even so, nothing but good can be expected from the abandonment of the purely symptomatic schemes of classification now obscuring our outlook on the disease. For fuller information on the manifold clinical aspects of lethargic encephalitis in the outbreak of the past six months in France the reader is referred to the *Bulletins et mémoires de la Société médicale des hôpitaux de Paris*, January–June 1920, and to *Medical Science*, 1920, **2**, 403.

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F. M. R. W.

ABSTRACTS

NEUROLOGY

Pierce Clark, L. A psychological interpretation of essential epilepsy. *Brain*, 1920, **43**, 38.

Our ignorance of the causes and nature of epilepsy is so profound and our impotence to control its manifestations effectively so disheartening that any attempt at a new approach to the problem will command attention. In the present paper Pierce Clark gives a *résumé* of his published observations on the psychological aspect of epilepsy. In his first chapter he expresses the conclusions derived from his own studies and from those of workers on similar lines as follows: there is 'a more or less constant' affective disturbance in all epileptics due to the 'inherent make-up of the psyche', which is characterized by egocentricity and hypersensitiveness. Unless these defects are corrected, permanent intellectual and emotional deterioration results. This epileptic alteration is evident long before the convulsive stage of the malady, which is but its final unfolding, is reached. At each of the stressful epochs of the epileptic's life his maladjustments to circumstances are particularly manifest. In a second chapter Clark traces him throughout life and describes these abnormal reactions. We are introduced here to the conception of the 'potential epileptic', whom Clark thinks it possible to detect by various minor abnormal reactions before any fit has occurred. At birth the potential epileptic child is unduly irritable and sensitive. Thus, one child 'fretted continuously at the contact of rough clothing', another 'cried continuously during the first three months' though nothing was found to account for it, yet another would not go to sleep unless rocked, while his last example is that of a child who 'nearly went into spasms at the sound of an air-brake'. Here we get a glimpse of the kind of foundation upon which Clark's 'psychological interpretation' is based.

In later infancy, with normal physical and intellectual development, defects of behaviour are seen, and there follows what all will recognize as a graphic account of the thoroughly spoiled and unmanageable child. During adolescence and adult life the epileptic shows an increasing degree and diversity of emotional defect arising out of his egocentricity and hypersensitiveness. It is not possible in a short review to describe details of this, though to appreciate the value of Clark's theories it should be studied in full. As to whether the epileptic's intellectual endowments are similarly disordered, Clark's statements are very conflicting and nothing definite on this point can be deduced from his paper.

'Given this inherent defect of make-up,' Clark says, 'it is easy to comprehend how all forms of undue physical and mental stress may operate deleteriously upon the epileptic. The gradations of epileptic reactions vary from day-dreaming, lethargies, petulance, sullenness, and outbursts of impatience, until there succeeds a series of minor attacks or a severe major convulsion.' The actual fit is simply the most extreme of the epileptic reactions, and is to be regarded as a protective mechanism by which the epileptic takes refuge from the intolerable stresses of an environment to which he cannot adjust himself, by a lapse into unconsciousness and a convulsion. The convulsion itself is compared with the movements of the foetus *in utero* and with those of the new-born child, and Clark expresses his conception of the motor convulsion as follows: 'the essential nucleus of the epileptic fit is an infantile unconscious striving of pleasure-displeasure ending in the final goal of a return to infancy . . . the convulsion is made up of and flows out of the general striving of the foetal and infantile tissues as expressed through the lower spinal centres', and again, 'we must therefore conclude that essential epilepsy as regards causation is dependent upon a primary congenital defect or inheritable defective instincts of natural and healthful adaptations to reality, the epileptic make-up or constitution, and that at successive periods of life, when emotional and physical stresses of an intensive character are encountered, the individual so constituted has epileptic reactions. . . . The fit is essentially a regressive phenomenon, a flight from undue stress into unconsciousness,' and finally, 'at first the epileptic strives to rid himself of an onerous task or unpleasant companions: sexual strivings are uncovered and in the deepest level he has made a retreat to the home, is in the cradle or the mother's arms, &c.'

The task which Clark has set himself is undoubtedly one of extreme difficulty and complexity, demanding as it does not only a sound knowledge of psychology and much clinical intuition, but also an appreciation of physiological principles. Judged by this high but essential standard, it is open to question whether he has succeeded. To the general physician, who is daily faced by this problem, perhaps the most obvious weakness of the hypothesis is the conception of the 'potential epileptic'. To have any value this must convey a clear-cut picture of abnormal reaction and behaviour peculiar to epilepsy, derived from the careful study of a large series of potential epileptics in whom epilepsy, as the term is commonly understood, later appeared. Clearly, a delving into the remote past of frank epileptics by an observer looking for facts to fit his theory has slight value by itself. Unfortunately, Clark does not state the proportion of potential cases studied by him in whom his opinion received confirmation in this way. Moreover, it is hard to believe that, had he really understood the human child in health and disease, and had he approached the problem with an open mind, he could have seen the portents he does in what might equally well have been physiological reactions to inefficient nursing and bad training. Surely, too, had ordinary observation failed him, a knowledge of the physiology of motor co-ordination would have prevented him from comparing the movements of the healthy and contented baby with the epileptic convulsion.

While all that he says of the egocentricity and hypersensitiveness of the epileptic may be just, is there anything in it at all peculiar to epilepsy? A careful analysis of the data recorded in the description of potential epilepsy reveals no single feature or combination of features by which the disease could be recognized before the occurrence of a fit. In fact, the application of such a theory could only be fraught with danger, and in its present form it is of no practical value.

Though cast on lines that are now somewhat familiar, Clark's explanation of the nature of the epileptic convulsion is extremely obscure. Phrases borrowed from clinical pyschology, figurative expressions, and fragments of physiological terminology jostle one another in an inextricable confusion, as may be seen from the passages quoted earlier.

If the exact meaning of this hypothesis and its bearing on the phenomena of a convulsion seem very obscure to most clinical observers, their difficulty will be considerably increased when they attempt to apply it to the case of the convulsions, so frequently indistinguishable from the idiopathic variety, arising in the course of certain toxaemias and in diffuse and focal structural disease of the brain.

As to the practical result to be expected from this theory, built as it appears to be upon such slight and insecure foundations, it is not easy to be optimistic. Clark has apparently given several years to the study of the question, but he still confines himself to a discussion of therapeutic possibilities. The position was well expressed in a recent review of this subject at the Royal Society of Medicine (*Sect. Neurol.* 1919–20, **13**, 1) as follows: 'Any method or remedy that will strengthen the adaptive power of the epileptic to the strains and stresses of life is to be sought out and made available, but nothing which has been mentioned has shown the need for discarding the use of small and carefully regulated doses of the bromides in suitable cases.' F. M. R. W.

(1) **Franz, S. I., Scheetz, M. E.,** and **Wilson, A. A. The possibility of recovery of motor function in long-standing hemiplegia.** *J. Am. M. Ass.*, 1920, **65**, 2150.

(2) **Ogden, R.** and **Franz, S. I. On cerebral motor control: the recovery from experimentally produced hemiplegia.** *Psychobiology*, 1917, **1**, 33.

(1) The authors discuss the imperfect recovery of function in the limbs, particularly in the arm after hemiplegia from cerebral lesions. Such restoration of function as occurs ensues within a few months and probably results from resolution of clot and from the clearing up of diaschisis.

The residual paralysis and the contracture have commonly been regarded as incapable of improvement. As a result of some animal experiments, Franz concluded that the permanence of paralysis in these circumstances was not inevitable, but was the result of inadequate treatment.

Five long-standing spastic residual hemiplegias were therefore subjected to special local treatment. Three methods were adopted. The first was that of massage and vibration. Effleurage and stroking was used for the spastic flexor groups in the arm, and the whole limb was shaken or vibrated until there had been a distinct loosening of the muscles. The weaker extensor groups were given tapotement and passively stretched. These two methods made possible the third and most important, which was that of inducing the patient to use the limb voluntarily in simple forms of action. Often several weeks of passive treatment were needed before active movements became possible.

In every case the results were most favourable and showed the possibility of return of useful function in a paralysed limb long after the condition had been regarded as residual and permanent. They conclude that every effort should be made by forms of local mechanical treatment, applied early and persisted in, to make some form of voluntary activity possible. When this has been achieved and the patient can be induced to co-operate, functional restoration of real usefulness may often be obtained.

(2) These observations suggested that if the limbs of an experimentally paralysed animal were properly dealt with recovery would be more rapid and complete than if the animal were left entirely to its own devices.

Four male macaque monkeys were used. Hemiplegia was produced by the application of the electro-cautery to the motor cortex, which was previously delimited by electrical stimulation. In each instance flaccid hemiplegia resulted.

It was found that, if the monkey were untreated, recovery after six months was very slight and considerable disability remained. If ordinary massage were used there was more, but still slow and partial, recovery. If the sound arm were confined by a jacket and the animal compelled by various tricks to use the paralysed arm frequently in various simple purposive acts and also to exercise the lower limb, recovery was very rapid, and after three weeks was apparently complete. Massage (friction and tapotement) were employed in addition to stimulating the animal to active movement.

In all, seven hemiplegias were produced in four animals, and it was clear that stimulation to active movement, confinement of the sound limbs, and massage rendered certain rapid and early recovery, when neglect or the ordinary treatment of the clinician was strikingly ineffectual.

These observations raise the whole question of whether voluntary movements can be carried out through other channels than the precentral cortex and the pyramidal fibres arising therefrom. F. M. R. W.

Pardee, I. H. An acute descending radicular type of epidemic encephalitis. *Arch. Neurol. & Psychiat.*, 1920, **4**, 24.

Pardee reports eight cases of a febrile illness characterized by symptoms referable to a radiculitis of a descending distribution, which appears first in the upper cervical region and spreads by a series of leaps to the sacral. Three of the eight had also the usual signs and symptoms of lethargic encephalitis: lethargy and signs of a midbrain lesion. The affection begins with paraesthesiae and pains in the neck and shoulders; these soon spread to the arms and may be severe and accompanied by extreme cutaneous hyperaesthesia. In a few days involuntary muscular spasms of the tremor variety appear in the head and neck and then in the arms and hands. When these are affected the spasms may render the limbs useless for voluntary movement, and they also persist during sleep.

When in the course of a week this symptom-complex is established, delirium appears with hallucinations and confusion. This lasts for a few days and gives place to marked apathy, which Pardee is at great pains to distinguish from lethargy.

During the second week of the illness the symptoms proceed to involve the thoracic posterior roots. Girdle pains round chest and abdomen, spasmodic contractions of the corresponding muscles develop, and after a further pause of three or four days the lumbo-sacral roots are affected, with the onset of pain, hyperaesthesia, and muscular spasms in the lower limbs. Apparently a recrudescence of fever and delirium heralds each advance of the malady.

In five of the cases there was no lethargy, no cranial nerve palsies, no objective sensory loss, and very little weakness. The reflexes were not materially affected, though the tendon-jerks varied in facility from day to day.

A moderate leucocytosis in the blood and a slight increase of lymphocytes and globulin in the cerebrospinal fluid were noted. This meningeal reaction does not seem to have been at all marked.

All the cases occurred during January or February of this year in Philadelphia. None of the uncomplicated cases died. There was a considerable amount of influenza at the time, but no definite history of the malady in the reported cases.

Pardee reviews the literature of lethargic encephalitis for cases bearing a resemblance to his, and speculates as to the relationship between them and the various symptom-complexes attributed to lethargic encephalitis, and he concludes that acute descending radiculitis is a form of this malady.

F. M. R. W.

Weisenberg, T. H. Poliomyelitis: a study of the 1916 Philadelphia epidemic, with a report of 717 cases. *Tr. Am. Neurol. Ass.*, 1918. (*Arch. Neurol. & Psychiat.*, 1920, **3**, 665.)

Of the total just over half were males. The ages ranged from under six months to over 30 years. 63 per cent. were under three years, and the total mortality was 23 per cent.

The preparalytic symptoms are considered in detail. Fever was constant, ranging from 100 to 103 with but slight diurnal variation and persisting for not longer than a week. The pulse and respiration rates ran parallel with the temperature. Nausea and vomiting were common; delirium, convulsions, or stupor rare. Objectively, during this stage, the phenomena of a meningitis were present.

The onset of the paralysis occurred on the second or third days and rapidly reached a maximum. Relapses were not seen. Pains, ascribed to meningeal irritation, in the head, neck, and back were constant, and subsided when the other meningeal symptoms abated, or after lumbar puncture.

The paralysis varied and is classified into the usual groups. Cranial nerve palsies and cerebellar symptoms were characterized by their relatively rapid recession, and in limb paralyses it was noted that the distal segments of the limbs regained power first.

The cerebrospinal fluid was invariably under pressure and was clear or faintly opalescent. During the first two weeks of the illness a moderate lymphocytosis was present, and in a few cases a fibrinous coagulum on standing. An increase of globulin was present in a third of the cases and the colloidal gold test gave a meningitic reaction in about half.

Of the various methods of treatment of the acute infection used, none appear to have given any definitely good result. There was little evidence of personal contagion.

F. M. R. W.

Da Fano, C. Recent experimental investigations on the aetiology of disseminated sclerosis. *J. Nerv. & Mental Dis.*, 1920, **51**, 428.

Da Fano reviews all recent work and concludes that by injecting cerebrospinal fluid and blood from typical cases of disseminated sclerosis various investigators have been able to produce in rabbits and guinea-pigs a disease of the nervous system ending, after a variable incubation period, in paralysis and death. Intraperitoneal injections gave the best results in guinea-pigs and intra-ocular injections in rabbits. The fluids from a given case did not always give positive results if withdrawn at different times. There is some evidence that this experimental disease is transmissible from animal to animal.

The lesions found in the cords of affected rabbits resemble those of disseminated sclerosis, while in the blood, in the vessel walls, and in the cerebrospinal fluid an apparently specific spirochaete has been found. In a human case a similar living spirochaete was found two hours after death in the brain. The lesions may be due not only to a living virus but also to a toxin formed by it. As yet we cannot finally accept the view that disseminated sclerosis is due to infection by a specific spirochaete.

F. M. R. W.

Weinberg, F. u. Hirsch, F. Hemiatrophia facialis bei chronischen Lungenaffektionen, ein Beitrag zur Ätiologie und Pathogenese des Leidens. [**Facial hemiatrophy in chronic lung disease.**] *Deutsche Ztschr. f. Nervenh.*, 1920, **66**, 204.

Although commonly said to occur as a sequel to the acute infectious fevers, particularly those of childhood, there is no convincing proof that this is true of facial hemiatrophy.

The authors report six cases of the affection, in four of which there was an accompanying palsy of the cervical sympathetic on the same side. In every case there was a chronic pleurisy with thickening of the pleura and fibrosis of the lung on the same side of the body as the facial affection. In every instance the facial hemiatrophy appeared soon after the onset of the pulmonary disease and progressed with it.

They suggest that the lesion of the pleura and lungs is the immediate cause of the cervical sympathetic paralysis and that this in turn gives rise to the hemiatrophy. F. M. R. W.

Cobb, S. Electromyographic studies of muscles during hysterical contractions. *Arch. Neurol. & Psychiat.*, 1920, **4**, 8.

By the use of the string galvanometer Cobb has studied the action currents of muscles in normal and in hysterical contractions. He finds that the resulting electromyograms in both conditions are similar and that tremors of hysterical character can be distinguished from such organic tremors as occur in paralysis agitans and from organic clonus by their slower rate and greater irregularity. F. M. R. W.

Stopford, J. S. B. The results of secondary suture of peripheral nerves. *Brain*, 1920, **43**, 1.

The paper contains an analysis of 271 cases of secondary suture of peripheral nerves. Most of the patients were under continuous observation for varying periods up to three years after operation, and the monthly progress is shown by means of twelve charts. The principal conclusions resulting from the study of these patients can be most conveniently tabulated in four groups.

I. Factors which may influence the prognosis:

(1) Sepsis.

(2) Site of the suture, the prognosis being more favourable the nearer the suture is to the spinal cord.

(3) A delay of more than eighteen months before the suture is performed in the distal part of a limb prejudices the chances of recovery, but is not of so much consequence in the proximal part.

(4) 'Bad-shunting' is probably a common cause of imperfect recovery in such nerves as the ulnar.

(5) Destruction of branches of the nerve, in addition to injury to the trunk, may be a cause of incomplete recovery.

(6) Ununited fractures, especially of the humerus in injuries to the musculospiral, are a serious complication. Evidence appears to be in favour of primary fixation of the bone.

(7) Ligature of the main artery in the proximal part of a limb may delay and limit recovery.

(8) Imperfect recovery of afferent fibres from such structures as joints, muscles, and tendons, is probably an important cause of limited functional recovery of the hand for the performance of purposive actions, although the voluntary power of individual muscles may be good.

II. The intrinsic muscles of the hand and the muscles in the distal part of a limb recover less frequently than the larger muscles in the proximal part of a limb. Probably several factors contribute to the cause of this:

(1) Distance which the young nerve fibrils have to travel away from their trophic centre in the spinal cord to reach the muscle.

(2) The size of the nerve of supply. The larger the nerve the greater the chance the young fibrils must have of reaching the muscle.

(3) Possibly the phylogenetic history of the muscles, since there does seem to be some support of the hypothesis that more recent acquisitions are the more vulnerable.

III. The following points bearing on the surgical technique can be deduced:

(1) It is advisable to avoid the through and through suture, whenever practicable, as proved also by the experimental work of Sargent and Greenfield.

(2) The construction of a new bed for the nerve, after suture, is preferable to any autogenous or heterogenous protective material. The unsatisfactory bed after suture of the external popliteal nerve, in the vicinity of the head of the fibula, is probably a cause of many failures.

(3) Displacement of the ulnar nerve in front of the internal condyle of the humerus, or widespread freeing to procure apposition of the ends, does not appear to retard the recovery.

(4) Liberal resection of the injured ends is essential and particularly necessary if sepsis is prominent.

IV. No recovery after the performance of secondary suture could be regarded as perfect. The chief causes of the imperfect result after *secondary* suture appear to be:

(1) The fact that an appreciable portion of the nerve-trunk has to be resected causes inevitably a disturbance of the intraneural anatomy, however carefully the surgical procedure is carried out.

(2) After secondary suture the nerve is making a *second* effort to regenerate, the first attempt being represented by a neuroma or outgrowths along fascial planes.

(3) The almost constant occurrence of one or more of the foregoing factors which have been found to influence the prognosis.

J. S. B. S.

PATHOLOGY AND BACTERIOLOGY

Blake, Francis G., and **Cecil, Russell L.** **Studies on experimental pneumonia. I. Production of pneumococcus lobar pneumonia in monkeys.** *J. Exper. M.*, 1920, **31**, 403. **II. Pathology and pathogenesis of pneumococcus lobar pneumonia in monkeys.** *J. Exper. M.*, 1920, **31**, 445. **III. Spontaneous pneumonia in monkeys.** *J. Exper. M.*, 1920, **31**, 499. **IV. Results of prophylactic vaccination against pneumococcus pneumonia in monkeys.** *J. Exper. M.*, 1920, **31**, 519.

Cecil, Russell L. and **Blake, F. G.** (1). **Studies on experimental pneumonia. V. Active immunity against experimental pneumococcus pneumonia in monkeys following vaccination with living cultures of *Pneumococcus*.** *J. Exper. M.*, 1920, **31**, 657.

Cecil, Russell L. and **Blake, F. G.** (2). **Studies on experimental pneumonia. VI. Active immunity following experimental pneumococcus pneumonia in monkeys.** *J. Exper. M.*, 1920, **31**, 685.

These are the first six of an important series which, the authors tell us, will run into ten papers, and they deal with various aspects of pneumonia, artificially produced in monkeys, by inoculation with cultures of *Pneumococcus* and other organisms. In the first communication they describe the results in 37 monkeys (*Macacus syrichtus* and *Cebus capucinus*) injected intratracheally with minute amounts of cultures of one or other of the four types of pneumococcus, but especially Type I. Under aseptic precautions a small calibre, dry, sterile needle was introduced into the lumen of the windpipe between the cartilages and just below the larynx, and through the needle the culture was injected from a glass syringe which fitted the stock of the needle. The amounts of culture injected varied from 0·000001 c.c. to 1 c.c. grown for 18 hours in plain broth. Of the 37 animals inoculated in this way only 5 failed to show pneumonia. Positive results were obtained with all four types of *Pneumococcus*, protocols being given in the text of the paper which show that the disease was clinically identical with that seen in man. In one case the disease was propagated by contact. Four healthy monkeys had living cultures of virulent pneumococci sprayed into the nose and mouth in quantities of 2 to 4 c.c., but no symptoms were produced. The pneumococcus was proved to be present in the saliva for a period of a month after the experiment was begun. The authors discuss the origin of pneumonia on the basis of these results, and decide on the aerogenic (bronchogenic) rather than on the haematogenic hypothesis. The latter view has been based chiefly on the extent of the pulmonic lesion in early cases of pneumonia and on the occurrence of pneumococci in the blood at the time when the clinical symptoms first made their appearance. In their own experiments the authors found that pneumococci may be present in the bloodstream from 6 to 24 hours after intratracheal injection and frequently before any evidence of symptoms. They think that the blood infection takes place by the way of the lymphatics draining from the lungs—a supposition supported by a study of the earliest morbid experimental lesions. The failure to produce pneumonia by instilling cultures into the mouth and nose suggests that there are special factors which determine the invasion of the bronchi with consequent pneumonia. What these factors are was not elucidated. Subcutaneous or intravenous injection of pneumococcus did not lead to pneumonia, the animals having died of septicaemia or recovered without evidence of pulmonic localization. Blood counts showed a marked polynuclear leucocytosis beginning 6 hours after inoculation and reaching an acme within 24–48 hours. In some cases it was well developed before there was any other sign that the infection had succeeded. The authors interpret the initial leucocytosis as an immediate response, on the part of the animal, to combat the infection at the site of entry. In the case of a monkey which showed a rise of polynuclear leucocytes and was killed within 3 hours after intratracheal injection, histological sections showed extensive infiltration of leucocytes in the peribronchial tissue near the hilum, and many of them had already passed into the lumen of the bronchus. Following the primary leucocytosis there is a constant fall, the rapidity and extent of which seemed to have direct relation to the severity of the disease and the degree of blood invasion.

The second paper, illustrated with 23 plates containing 35 excellent figures, deals with the macro- and microscopic changes in 40 cases of pneumonia induced experimentally in monkeys by intratracheal injection of cultures. The lesions were identical with lobar pneumonia in man. A careful study led the authors to the view that the pneumococcus primarily invades the tissue of the lung at some point or points in the portion of the lobe proximal to the hilum, that it rapidly spreads throughout the lobe by perivascular, peribronchial, and septal interstitial tissue and lymphatics, quickly reaching the pleura, and that it invades the alveolar structure primarily by way of the alveolar walls, subsequently passing into the alveolar spaces themselves with outpouring of the inflammatory exudate. Although there is a possibility that primary invasion may occur in terminal bronchioles, alveolar ducts, or alveoli of the parenchyma near the hilum, the authors consider that evidence is against this view. They consider that lobar pneumonia is primarily an interstitial infection of the lung. Hepatization begins in alveolar tissue proximal to the hilum, and progressively spreads to the more distal tissue until complete lobar consolidation develops. By degrees, the conspicuous interstitial changes of the earliest stages diminish or become masked in the general solidification. In the monkey, resolution is often accompanied by a degree of organization of the grosser framework of the lung, and a certain amount of organization of the alveolar exudate is occasionally seen.

The third communication deals with a spontaneous outbreak of 36 cases of pneumonia which occurred in two out of three lots of monkeys imported into Washington from the Philippine Islands for experimental purposes. In the first lot of 19 monkeys there were 8 cases of pneumonia; in the second lot of 79 monkeys there were 28 cases, while in the third lot of 46 animals, which had been carefully segregated, pneumonia was absent.

Of the total 36 cases of the disease, all but three occurred after the arrival of the second lot of monkeys, and although the original source of the epizootic was not determined, there was abundant evidence that it was spread chiefly by contact. In its clinical features, complications, and pathology the spontaneous disease was identical with the lobar pneumonia produced experimentally by intratracheal insufflation of cultures or the disease in man. Bacteriologically, *Pneumococcus,* Type IV, was found 28 times in 32 cases which could be satisfactorily examined. *Streptococcus haemolyticus* was found in 2, a non-haemolytic *Streptococcus* of the *viridans* group in 2, with *Streptococcus haemolyticus* in 1 case. The immunological reactions of the pneumococci isolated were examined, three rabbits having been immunized with three separate strains. Of 21 strains of pneumococci examined, 9 were agglutinated by one of the sera, and 5 by another, leaving 7 strains which did not fall into any of the groups. It is interesting to note that 5 cases of fatal pneumonia, apparently contracted by contact, died in 9 days, and the strains of pneumococci isolated from them were all agglutinated by the same immune serum. Twelve plates with 16 figures illustrate the identity of the spontaneous pneumonia with the experimentally produced disease.

The fourth investigation deals with attempts to produce an active immunity against pneumonia in monkeys, evoked by intratracheal inoculation of virulent pneumococci, and bears on the question of the use of prophylactic vaccines in man. In their experiments the authors employed a monovalent vaccine prepared from an old stock-culture of Type I, the infecting culture being a highly virulent one of the same type which was lethal to mice in doses up to 0·00000001 c.c. Of this culture 0·000001 c.c. produced pneumonia in monkeys. A lipovaccine was prepared by collecting the pneumococci, in an 18-hour-old broth culture, by means of the centrifuge. The cocci, being dried at 55° C. for 24 hours, were ground up by steel balls, the dry powder being finally suspended in cotton-seed oil containing 2 per cent. lanolin and diluted to the desired strength. The dose administered to the monkeys was $\frac{1}{16}$ of that which had been utilized for the immunization of soldiers in the Army Medical School, Washington. Neither small nor large doses of Type I lipovaccine protected monkeys against subsequent attacks of Type I pneumonia either spontaneous or experimental. Further, a number of monkeys that had been vaccinated with Type I vaccine, and were put into a large cage with a number of stock monkeys, developed Type IV pneumonia which had broken out spontaneously in the cage. A study of the protocols appended reveals the fact that the vaccination modifies the course of the disease, the septicaemia in the vaccinated animals being slight and the proportion of recoveries being higher as compared with unvaccinated animals.

A second series of protective experiments was made with pneumococci heated to 55° C. for an hour and suspended in saline containing 0·25 per cent. tricresol. Although this also failed to produce immunity against intratracheal inoculation there was evidence that it was a better antigen than the lipovaccine used when vaccinated animals were subsequently inoculated *intravenously* with pneumococci; there appeared to be very definitive protection in comparison with the controls, which developed a heavy septicaemia. This led the authors to the view that a distinction must be made between a humoral immunity against pneumococci and a local immunity, possibly cellular, in the lungs. The same dose which vaccinated animals withstood when the culture was administered intravenously would have produced a severe pneumonia if given into the trachea. The authors issue a warning against transferring these conclusions to the domain of human pathology without further investigation, for there can be no doubt that the monkey is much more sensitive to pneumococcus than man, in whom a gradual immunity develops, probably by reason of repeated exposure to pneumococci from birth onwards.

The fifth paper deals with the active immunity against experimental pneumococcus pneumonia induced by inoculation with living cultures of *Pneumococcus*. It will be remembered that the earliest attempts of Pasteur to produce a prophylaxis against chicken cholera, rouget des porcs, anthrax, and rabies, were carried out with the living attenuated virus, and were demonstrated to be exceedingly effective. The method, however, with the exception of rabies, was not applied to man on account of the possible risk of death. Practically all the prophylactic vaccination methods for human beings have been carried out with killed cultures, the efficacy of which was demonstrated by Salmon and Smith. There has, however, always been the feeling that with the destruction of the virus some important immunizing principles were lost, so that the immunity produced by killed cultures was less potent than when living cultures—even attenuated cultures—were used as the antigen. Haffkine inoculated large numbers of human beings, in India, with living cultures of *Vibrio cholerae* with encouraging results, while a similar process was adopted by Strong, in Manila, in the case of *B. pestis*. The present authors have now applied the principle of using living cultures of *Pneumococcus*, Type I, and have compared the effects of virulent and avirulent strains, injected subcutaneously, in preventing pneumonia from the subsequent intratracheal injection of the homologous microbe. All the experiments were conducted in monkeys (*Cebus* and *Macacus*). Of the virulent broth cultures 0·001 c.c. (about 400,000 pneumococci) was injected. In vaccinating with avirulent cultures a dose of 1 to 2 c.c. undiluted broth cultures was employed. A somewhat detailed account of the history of a monkey injected with 0·001 c.c. of a virulent living culture subcutaneously showed that there was a sharp rise of temperature but no leucocytosis. Blood cultures taken at daily intervals showed that the injected pneumococci had invaded the blood-stream within three hours, and at the end of 24 hours 1,000 colonies of cocci were counted from 0·5 c.c. of blood. In spite of the undoubted septicaemia the monkey did not appear to be very ill and in five days was well. Twenty days after the inoculation its serum protected mice against 1,000 multiples of the minimal lethal dose of pneumococci. That the injection of living virulent cultures is risky was shown by the fact that at least one monkey succumbed with a heavy blood infection. In one animal that had been vaccinated with virulent virus an intratracheal injection of 100,000 times the minimal infecting dose was without result, whereas a control animal succumbed with incipient lobar pneumonia and profound septicaemia the day following the inoculation. Cross-immunity experiments, in which *Pneumococcus*, Type II, was injected intratracheally after a vaccinating subcutaneous dose of Type I showed that the latter had created a certain degree of immunity towards the former. The same was found to be true with Types II, III, and, to a less extent, Type IV, although there were considerable individual differences. An interesting observation is related where a monkey vaccinated with virulent *Pneumococcus*, Type I, developed spontaneous pneumonia due to Type IV fifteen or sixteen days later. Experiments with living but avirulent cultures also showed a degree of active immunity equal to that produced by virulent virus, provided that the dose was sufficiently large (e. g. 2 c.c. of an 18-hour-old bouillon culture). The active immunity induced by both viruses appeared to be largely independent of the presence or absence of agglutinins and protective substances in the serum of the monkeys employed.

The sixth paper concerns experiments which were made to test the degree of active immunity in monkeys subsequent to an attack of experimental pneumococcus pneumonia from which they had recovered. Two monkeys inoculated with *Pneumococcus*, Type I, intratracheally, both developed the signs of pneumonia with positive blood cultures and leucocytosis. About three weeks later they were again inoculated intratracheally with the same culture and remained well, whereas two control macaques died of lobar pneumonia in three and seven days respectively.

An attack of *Pneumococcus* Type I pneumonia was found to give little if any protection against *Pneumococcus* Type II pneumonia. Experiments with *Pneumococcus* Type III were not conclusive. Of more importance were experiments where a first attack of pneumonia was induced with Type I, the animal being subsequently injected with Type IV. Immunity was not apparent. Further, experimental *Pneumococcus* Type IV pneumonia in monkeys conferred slight if any protection against subsequent infection with the same or with a homologous strain of Type IV. Type IV pneumonia likewise leaves no cross-immunity to a subsequent Type I injection intratracheally. It will be recalled that Type IV is not really a type analogous to Types I, II, and III, as it consists of a large number of pneumococcus strains which do not fall into the other three groups and which usually have no biological connexion with each other. It is alleged that certain individuals are prone to repeated attacks of pneumonia, and the authors make a suggestion that possibly these are due to Type IV, which, in the monkey, leaves little or no immunity. W. B.

Thomsen, O. et Kristensen, M. Recherches sur la bactériologie et l'épidémiologie de l'influenza de 1918–1919 (la Grippe espagnole). [**Researches on the bacteriology and epidemiology of the influenza of 1918–1919 (Spanish 'Flu.**] *Acta Medica Scandinavica*, 1920, **53**, 422.

The authors observed that, in the recent epidemic, young persons were attacked much more frequently than those over 30. They investigated two large banks and two shops. The total population of these establishments was 2,702 persons. Of those aged 20 or less 52 per cent. were affected, and the incidence fell as the age increased until at 61–70 only 3·9 per cent. were attacked. In order to determine whether this difference was due to an immunity remaining from the 1889–91 epidemic, the authors asked all the cases whether they had had the disease before, but the information supplied was unsatisfactory.

Discussing what features in a bacterium should allow its classification as *B. influenzae*, the authors define the characters of this bacillus, namely, the morphology, growth on horse-blood agar, dependence on haemoglobin, and symbiosis.

Varieties among these bacilli consist in a certain amount of deviation from the standard.

Using horse-blood agar *B. influenzae* was only demonstrated in a small number of cases, namely, in 35 per cent. From autopsies the bacillus was recovered in 51 per cent.

In the examination of the nasopharynx of healthy persons *B. influenzae* was found more frequently: in one batch of 22 men, in every case. It would appear that for these cultures the authors made use of another medium containing washed corpuscles. This medium produced much larger colonies. *B. influenzae* is found more frequently in normal persons or in persons suffering from other diseases than in influenza.

The authors reject *B. influenzae* as the cause of influenza and criticize the grounds upon which Pfeiffer introduced it.

The last part of the paper is taken up with a consideration of the mode of propagation of pandemics. P. F.

Bieling, R. u. Joseph, K. Immunisierungsversuche mit Influenzabazillen. [**Immunization experiments with influenza bacilli.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 228; 475.

A short study of the agglutinins, precipitins, bacteriotropins, bactericidal and complement fixing substances evoked by inoculations of *B. influenzae.* Three cultures were used in the experiments. Rabbits inoculated three times intravenously with quantities of $\frac{1}{10}$, $\frac{2}{10}$, and $\frac{4}{10}$ of a blood agar culture yielded sera of which the agglutination titre varied between 1:400 and 1:16000, a more constant and quicker high titre being obtained when the animals had pyrexia induced by exposure to a 1,000 candle-power metal filament lamp during the first three days subsequent to the inoculation. The horse was found less suitable for the production of agglutinating sera. The agglutination titre of the rabbit serum for various strains of *B. influenzae* was found to be more or less constant, although a number of inagglutinable or spontaneously agglutinable cultures were met with. High titre agglutinating rabbit sera also show specific precipitins. Although experiments were difficult to carry out, there was definite evidence of bactericidal substances in the immune sera both of rabbits and horses. In the presence of leucocytes of guinea-pigs, quantities of immune serum varying from 0·001 to 0·0001 c.c. were distinctly bacteriotropic, while the authors were also able to demonstrate specific complement fixation. The agglutinating and precipitating action of the serum on the one hand and the bacteriotropic and complement fixing action on the other appeared to run parallel.

In the second communication the authors make a more exact analysis of the agglutinating and absorbing property of the serum of rabbits immunized with *B. influenzae* and confirm results which have been found by some other workers. There exist monovalent strains of influenza bacilli the inoculation of which evoke the production of sera which agglutinate only the homologous strain. There are also, however, polyvalent strains, immune sera from which agglutinate not only homologous bacilli but also other polyvalent as well as monovalent bacilli. Among the polyvalent sera there are different types distinguished by the fact that they induce precipitation and absorb more agglutinin in the presence of the homologous polyvalent than in heterologous polyvalent strains. The receptors common to monovalent and polyvalent races are more thermolabile than the receptors, which differ in the various races. W. B.

Wolf, J. E. Beiträge zur Biologie des Pfeifferschen Influenzabazillus. Mischkulturen—Mischinfektion. [**Contributions to the biology of Pfeiffer's influenza bacillus. Mixed cultures and mixed infection.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I., 1920, Orig. **84**, 241.

This is a series of experiments carried out in culture media and *in vivo* to determine how *B. influenzae* behaves in the presence of other bacteria. In haemoglobin-containing media *M. catarrhalis* and *M. flavus* in particular, but also *Streptococcus, Pneumococcus, Staphylococcus, Meningococcus,* and *B. diphtheriae* encouraged the growth of Pfeiffer's bacillus, whereas *B. pyocyaneus* and *B. subtilis* retarded it. On haemoglobin-free media the influenza bacillus grew when in the presence of *M. catarrhalis* and *M. flavus.* Even cultures heated to 60° C. encourage *B. influenzae* to grow. Inoculations of influenza bacilli in mice and guinea-pigs did not lead to a blood infection, but by combination with streptococci or pneumococci cultures of both organisms were recovered from the blood.

W. B.

Bache, R. Leukocyttällinger ved Influenza. [**Leucocyte counts in influenza.**] *Norsk. Mag. f. Lægevidensk.*, 1920, **81**, 176.

In the winter of 1918–19 Bache carried out leucocyte counts in 206 cases of influenza, only 64 of which were uncomplicated; the rest were complicated by pneumonia, pleurisy, sepsis, or empyema. Two of his cases were particularly instructive. One was that of a man the number of whose leucocytes was subnormal on his admission to hospital. With the development of pneumonia and of numerous pneumococci in the blood, the leucocytes rose rapidly to 23,000. This number fell soon afterwards to 10,400. Just before empyema was diagnosed, the leucocytes rose to 15,600. In spite of the free growth of pneumococci cultivated from the blood, the patient recovered. The other case was also characterized by a low leucocyte count on his admission to hospital with pneumonia. As this progressed and empyema developed, the leucocytes rose to 41,200. Generalizing, Bache makes out that influenza and influenzal pneumonia are usually associated with leucopenia which, with the development of empyema, rapidly gives rise to marked leucocytosis. The mortality from pneumonia with a high leucocyte count seems to be lower than with a low count.

C. L.

Koga, G. and **Otsubo, I.** **On the spirochaeta-like bodies appearing in the culture of certain species of bacteria.** *Kitasato Arch. of Exper. Med.*, 1919, **3**, 207.

During an investigation of certain spirochaetes found in smegma the authors observed numerous spirochaete-like bodies developing in the cultures of a certain species of bacterium. Under dark-ground illumination or in China ink they were found to be very similar to the involuted forms of *Spirochaeta macrodentium* which Noguchi cultivated, in association with a certain species of bacterium, from the mouth. The bodies in question were 15–30 μ long by 0·3 to 1·3 μ wide and provided with 7–15 spirals. Some individuals, however, were several hundred microns long. In the dark ground they were found devoid of motion. Although these spirochaete-like bodies could be grown, they were not obtained pure. They could not be stained by aniline dyes, but with Loeffler's or Zettnow's flagellar stain they become deeply impregnated. Similar spirochaete-like objects were also obtained in association with *B. subtilis* and were found to be exceedingly thermostable and resistant to chemicals. The best medium for revealing the presence of the spirochaete-like bodies was one composed of horse-plasma and ascitic fluid. Horse-plasma was obtained by adding citrate of soda to the blood and allowing the corpuscles to settle. Equal parts of plasma and ascitic fluid of a total volume of 40·4 c.c. were then mixed with 1 c.c. of a 10 per cent. solution of chlorate (chloride ?) of calcium and the mixture was allowed to clot.

After inoculation the surface is covered with liquid paraffin and the tubes are incubated anaerobically. The authors believe that the spiral bodies represent either an abnormal development of the bodies of bacteria or more probably they are flagella in some special condition. *Bacillus subtilis* grown on ordinary agar for 20 generations showed only the ordinary bacillary form, whereas subcultures in plasma-ascitic fluid from each of these generations showed both bacilli and spirals. Similar spirals were produced in cultures of *B. typhosus*, *B. paratyphosus* A and B, *B. coli*, *B. proteus*, *B. murisepticum*, *B. tetani*, *B. pyocyaneus*, and *V. cholerae*. None were found in any cultures of cocci. Although *B. mallei* is always believed to be non-motile, spirals were found in cultures. W. B.

Reenstierna, J. (1). Ett serum mot mjuk chancre, speciellt dess buboner. [**An ulcus molle serum with special reference to cases complicated by bubo.**] *Förh. Svens. Läk.-Sällsk. Sammank.*, 1920, Hft. **3** and **4**, 47–50.

Reenstierna, J. (2). En mer än 1–årig ulcus molle-infektion läkt efter serumbehandling. [**Ulcus molle infection of over a year's standing cured by a serum.**] *Hygieia*, Stockholm, 1920, **82**, 270.

Reenstierna has obtained a serum from large rams inoculated intravenously with increasing quantities of dead and living cultures of the streptobacillus Ducrey-Krefting-Unna. This serum effected complement fixation down to 0·025 c.c. Its agglutinating capacity could not be ascertained with accuracy, as a suspension of this streptobacillus exhibits from the outset granular clumping. This serum has been tested in about 100 cases of ulcus molle, with buboes, at the Syphilis Clinic of the Karolinska Institute. After the intramuscular injection of 10 c.c. of the serum, enlarged and painful inguinal glands showed marked improvement as early as the following day. Having found with an antigonococcal serum that its effect in gonorrhoeal arthritis is enhanced when the patient's temperature is raised, Reenstierna has applied this principle to streptobacillus infection. To obtain a febrile reaction he combines his serum with killed, fever-promoting bacteria, such as typhoid bacilli.

With 7 exceptions, all his cases of bubo which had not burst or been incised terminated in recovery within an extraordinarily short time; the average duration of convalescence was somewhat over a week. As a rule he gave 2 injections, with an interval of 4 to 5 days. In no case did a relapse occur. As for the 7 cases which did not respond to this treatment, the swelling of the inguinal glands proved to be due to staphylococci in every case. These findings pointed to the specificity of the serum in relation to the streptobacillus of Ducrey. Reenstierna gives details of one case in which a suppurating inguinal bubo had proved refractory to surgical and other treatment for more than a year. Its cuti-reaction to a streptobacillus vaccine was definitely positive, and typical streptobacilli were found in the discharge from the bubo. A few days after the intragluteal injection of 15 c.c. of serum the wound showed definite signs of healing, and complete recovery was rapidly effected. C. L.

Kobayashi, R. and **Kodama, M. A contribution to the study of *Spirochaeta morsus-muris* in the Nippon field-vole (*Microtus montebelli*).** *Kitasato Arch. of Exper. Med.*, 1919, **3**, 199.

The authors have examined 17 strains of *Spirochaeta morsus-muris* obtained from man (2), the wild rat (1), and the field-vole (14). The last strains were obtained from field-voles (*Microtus montebelli*) in the Niigata and Saitama Prefectures in Japan. With reference to the incidence of the spirochaetes in field-voles they found a difference in that 12 per cent. of voles in Niigata were infected and 54 per cent. in Saitama. Further, the Niigata strains are not pathogenic for Japanese monkeys, whereas the Saitama strains are. Immunity experiments also indicated that there are distinct differences between these two strains. W. B.

Worms, Werner. Experimentelle Beiträge zur spezifischen Immunodiagnostik der Syphilis (Kutireaktion und Komplementbindung). [**Experimental contributions to the specific immuno-diagnosis of syphilis. (Cuti-reaction and complement fixation.)**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, **29**, 357.

This is an exhaustive study of the literature which has arisen on the relative merits, in the diagnosis of syphilis, of the cutaneous reactions from spirochaetal extracts and the Wassermann test. The author's own experiments were made with diverse extracts obtained from cultures of *Spirochaeta pallida*, the extracts being subsequently injected intradermically. The author favours in particular the method of extraction elaborated by Schereschewsky and his co-workers, and finds that the cuti-reaction agrees with the Wassermann reaction in 87 per cent. of the cases. Careful examination of the remaining 13 per cent. gave an indication in favour of the cuti-reaction. An extensive bibliography accompanies the paper. W. B.

Kuhn, Philalethes u. **Steiner, Gabriel.** Ueber die Ursache der multiplen Sklerose. [**On the cause of disseminated sclerosis.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 417.

In 1917 the present authors (*Med. Klin.*, 1917, **13**, 1007) described results which followed in rabbits and guinea-pigs inoculated with the blood and C.S.F. from 4 cases of disseminated sclerosis in man. They considered that they had successfully transmitted the disease, and in the affected animals they drew attention to the existence of certain spirochaetes. Of the 4 cases employed to supply the material 3 were early (4 months, 3 months, and 6 weeks respectively), while one had existed for years. Since then they have had the fortune to study 9 additional cases, 6 of which had lasted a long time, 3 being of recent origin. One of the 6 cases had an acute exacerbation of symptoms. Positive results were obtained in 1 guinea-pig out of 5 inoculated from this old case, and in 1 rabbit out of 5 inoculated from 1 of the 3 recent cases. Both by staining and by darkground illumination, spirochaetes (*S. argentinensis*) were found in the blood during life and in the vessels of the organs removed immediately after death. While considering the possibility that the spirochaetes may be accidental, the above facts incline the authors to the view that they may be the cause of the disease. In their first paper (*vide supra*) the authors referred to a monkey inoculated in March 1917. The subsequent fate of this animal is given in the present communication. At first, the inoculation, which was intraperitoneal, seemed to have been without the desired effect, but in February 1918 it was observed to have a fleeting paresis, which disappeared, to recur again in June 1918. It affected the hind limbs and lasted till July 1918, when the animal was killed. The hind limbs could not be used in locomotion and were flexed when the animal was held up. The reflexes were lively. With the exception of macroscopic foci in the brain, no lesions were observed at the autopsy. Microscopic sections (figured in two plates) led the authors to the conclusion that the lesions were identical with those found in human disseminated sclerosis. There was degeneration of the medullary sheaths in the foci, which were round, oval, or streaky, and occasionally confluent. Granular cells with lipoid contents and proliferation of the glia were marked features of the lesions, which occurred in the white matter of the hemispheres alone. Spirochaetes were, however, not detected. W. B.

Griffith, F., Scott, W. M., and **Eastwood, A. The complement-fixation test in syphilis, commonly known as the Wassermann test.** *Rep. on Pub. Health and Med. Subjects*, No. 1. Ministry of Health, London, 1920 (H.M. Stationery Office).

This Report contains such a mass of experimental data of a highly technical nature that it is unfitted for detailed review.

During the war the Pathological Methods Committee appointed by the Medical Research Council endeavoured to introduce some uniformity into the methods in vogue for carrying out the Wassermann reaction, and selected three prominent techniques for a 'blind' trial upon 100 cases of syphilis. Two of the selected techniques gave identical results, while the third corresponded closely. During the course of the discussions of this Committee certain principles of technique were found to differ in the practice of different workers and it was hoped that these differences might be overcome by further research. Dr. Griffith and Dr. Scott have made a protracted effort to attain this end, but they confess that they do 'not put forward any claim to finality'. Indeed this result is almost inevitable owing to the enormous opportunities for modifications and variations each one of which may vitiate the conclusions arrived at before.

The authors invite criticism and discussion, and therefore it may be permitted to express surprise that they have proposed such extensive departures from ordinary practice upon theoretical rather than practical grounds.

Some of the more unusual propositions are:

1. Inactivation of the test serum in a diluted condition.
2. Fixation in the ice-chest.
3. The use of a fixed quantity of complement.
4. The use of 'Noguchi's antigen' reinforced with cholesterin.

The testing of these modifications upon cases of syphilis will be arduous, and, in view of the accuracy of existing methods demonstrated by the

Medical Research Council, it is doubtful whether these proposals will receive as much examination as they deserve. The technical worker will, however, derive profit from a study of the detailed protocols introduced in favour of these departures.

Dr. Eastwood contributes a detailed critical survey of the principles involved in the test, illustrated by references to the works of foreign authors. P. F.

Gegenbaur, V. Das saprophytische Wachsthum von Milzbrandkeimen auf tierischen Haaren. [**The saprophytic growth of anthrax spores on animal hair.**] *Arch. f. Hyg.*, 1920, **89**, 202.

The author describes the results of a series of experiments in which sporing anthrax cultures were applied to the hair of animals either after removal or during life. He is of opinion that not only do the spores persist for considerable periods, but that multiplication actually takes place. The growth is favoured by the heat and moisture of the animal's coat in addition to various nutritive substances excreted in the sebum and sweat. Apparently the growth is a local one, as the bacilli do not spread to parts other than those at which the spore emulsion was applied. The occurrence of anthrax in hair from animals apparently healthy may be explained from contact with infected hides or anthrax-infected animals. W. B.

Reiter, Rupert. Über die Gewinnung resistenter Milzbrandsporen. [**On the preparation of resistant anthrax spores.**] *Arch. f. Hyg.*, 1920, **89**, 191.

In experiments to determine the value of disinfecting methods it is important to obtain the test bacterial material of the greatest resistance. One of the test objects most commonly employed is anthrax spores, which, according to the author, can be obtained in a maximal degree of resistance by growth on Heider's bran medium (*Arch. f. Hyg.*, 1892, **15**, 341). This is prepared by macerating 500 grm. of bran in 1 litre of water for 12–24 hours. It is then filtered and the filtrate is made up with 1·75 per cent. of agar and neutralized. Details are given of the resistance to steam of anthrax spores on this medium. W. B.

Stévenin, H. Le bacille court (Coryne-bacterium commune) et la diphthérie. [**The relation of the 'short bacillus' to diphtheria.**] *J. de physiol. et de path. gén.*, 1919, **18**, 568.

After an analysis, especially of the French literature, on the subject of the relation of diphtheria and pseudo-diphtheria bacilli, the author describes his own results on 20 strains of true diphtheria and 35 of pseudo-diphtheria bacilli (bacilles courts). All the long and medium sized bacilli grew anaerobically and gave Neisser's granules. Glucose and laevulose were always fermented, maltose and inulin were fermented by 10 out of 19 strains, lactose by 2 out of 19 strains. Mannitol and saccharose were never fermented. In the case of the short bacilli 25 out of 30 strains showed no Neisser granules, while 5 did. None grew anaerobically, and none of the sugars or alcohols above mentioned were fermented. None of the cultures were virulent or toxic. The author considers that

Coryne-bacterium commune (bacille court) has nothing to do with the causation of diphtheria. Studies of the incidence of the long and medium sized bacilli confirm this. He considers that the 'bacille court' is a simple saprophyte frequently found in the throats of people healthy and diseased. An analysis is given of the morphological and biological characters of 57 strains of 'bacille court' isolated from the throat, 1 from the skin, and 8 from water.
W. B.

Kolle, W. u. **Schlossberger, H.** Zur Pathogenität der Diphtheriebazillen. [**The pathogenic effects of diphtheria bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 193.

The authors tested the pathogenic effect, on guinea-pigs and mice, of 26 diphtheria cultures, 18 of which were isolated from the throat, and 4 from wounds; 3 were old laboratory strains and 1 was the famous Park-Williams strain. They confirmed the known fact that, when tested on guinea-pigs, cultures vary extraordinarily in virulence, and that the latter is not proportional to the toxin production. Instead of agar or broth cultures, the virulence was tested by means of 24-hour cultures on Loeffler's serum, the size of the dose of the living cultures being estimated in terms of a 1 mm. platinum loop. With this method the fatal dose for guinea-pigs was found to vary from $\frac{1}{5}$ to as little as $\frac{1}{500000}$ of a loop. Instead of subcutaneous inoculation the authors utilized a cutaneous method, the cultures being rubbed into an area of the skin depilated by calcium sulphide. By this method all the cultures proved virulent. Within 24 hours there was great redness and infiltration of the skin and death took place in two to three days with post-mortem appearances identical with those following subcutaneous injection of cultures. Extensive series of experiments were carried out on mice, which are well known to be very insusceptible to diphtheria toxin. The authors found that this was by no means the case when living cultures on serum were applied, doses of $\frac{1}{5}$ to $\frac{1}{50}$ of a loopful being fatal in three to eight days. Large numbers of bacilli were found at the site of inoculation, the suprarenal glands were congested, and diphtheria bacilli had almost constantly penetrated into the spleen. The extreme resistance of mice to diphtheria toxin was not due to the existence of any natural antitoxin content of their blood. The action of the living cultures depends on intoxicating properties, and it was supposed that, as the animals succumb to living cultures while being very tolerant to toxin prepared *in vitro* in the usual way, the toxins produced *in vivo* and *in vitro* could not be identical. It was found, however, that ordinary diphtheria antitoxin protects mice both against fatal doses of living cultures and against fatal doses of concentrated diphtheria toxin prepared *in vitro*. The serum of normal horses was unable to act in this way. W. B.

Müller, Hermann. Die Verwendbarkeit der intrakutanen Tuberkulinprobe zur Diagnose von Meerschweinchentuberkulose. [**The value of the intracutaneous tuberculin test in the diagnosis of tuberculosis in guinea-pigs.**] *Centralbl. f. Bakteriol.*, Abt. I., 1920, Orig. **84**, 256.

This investigation was carried out to determine whether it is possible to diagnose with certainty during life, by means of cutaneous inoculation of tuberculin, whether or not guinea-pigs have been successfully infected with tuberculosis. Ordinarily, after inoculation with suspected tuberculous material, the animals are killed in a month or six weeks and tuberculous lesions are sought *post mortem*. The author used calcium sulphide as a depilatory and subsequently injected intracutaneously 0·1 c.c. of a tuberculin dilution by means of a fine syringe into the bald area. As a result of 187 experiments with various tuberculins, human or bovine, he concluded that a positive reaction does not necessarily reveal a tuberculous infection. A negative reaction does not exclude tuberculosis with certainty. There were no marked differences with different kinds of tuberculin, and the author recommends a continuance of the old method of diagnosis above indicated.

W. B.

Shiga, K. (1). **I. Studien über das Tuberkulose-vaccin. Serovaccin aus den avirulenten, lebenden Tuberkelbazillen.** *Kitasato Arch. of Exper. Med.*, 1917, **1**, 157.

Shiga, K. (2). **II. Ueber die Frühbehandlung und Schutzimpfung bei Tuberkulose.** *Kitasato Arch. of Exper. Med.*, 1919, **3**, 239.

For a number of years Shiga has employed himself with the study of the influence of various chemical substances, especially dyes, on the tubercle bacillus, the object being to obtain strains of culture which should be non-toxic and at the same time easily absorbed. Ultimately, he found that certain strains are 'fast' to trypaflavin or erythrosin, i. e. they become acclimatized and remain uninjured when cultivated in solutions of these dyes. From these cultures he elaborated a sero-vaccine which could be employed for the prevention or treatment of tuberculosis in man and animals. The 'fast' strain was grown in broth, a small quantity of the bacilli being then removed from the medium, dried with filter-paper, and ground for 24 hours in an agate mortar. It was then mixed with a tubercle immune serum diluted with saline, the emulsion being first thoroughly agitated in a shaker and subsequently kept some hours at a temperature of 37° C. The emulsion was again centrifuged and ground in a mortar till the bacilli were completely pulverized. The bacillary emulsion was then suspended in saline containing 1 : 200,000 trypaflavin. Five milligrammes of the trypaflavin bacillary emulsion were then mixed with 1 c.c. of the bouillon filtrate of a culture of tubercle bacilli 'fast' to erythrosin, the mixture constituting Shiga's 'sero-vaccine'. This vaccine is very mild in its action and induces a phagocytosis round the tuberculous foci, ultimately leading to the proliferation of connective tissue with consequent arrest or cure of the lesion.

In the second paper he deals with the early treatment of tuberculosis of the lungs of human beings, by means of the sero-vaccine. He is strongly of opinion that cases should be treated in the earliest possible stages even although the existence of tubercle is suspected rather than proved. He considers that undoubtedly in Japan, and probably in other countries, the initial infection takes place in the family and mainly in childhood. Thus, from the Japanese statistics of 1917, he shows, for females, the acme of the tuberculosis incidence is reached between the 15–25 year, the highest incidence in males being 5 years later. In the last four years he has subjected 300 early cases to his sero-vaccine and from the results considers that it is a very active agent. The cases are first examined for Pirquet's reaction and the temperature is taken for a week before the proposed sero-vaccine treatment. The scheme of treatment suggested is as follows :

T. B. sero-vaccine	(1 : 5,000)	0·1	0·2	0·3	0·5	0·8
	(1 : 1,000)	0·2	0·3	0·5	0·7	
	(1 : 500)	0·5	0·7	1·0		
	(1 : 100)	0·25	0·4	0·7		
Living virus	(1 : 20)	0·2	0·4			

The living virus is a culture of trypaflavin-fast bacilli in 1 : 20,000 sol. of the dye. The idea is to create a 'ground' immunity with the sero-vaccine dilutions and complete the process with the living virus. Injections are made once a week over 17 weeks. W. B.

SCHMIT-JENSEN, H. O. En Mikroforgæringsmetode for den bakteriologiske Diagnostik og om Forgæringsprøver som Kontrol paa Kulhydratpræparaters Renhed. [**A microfermentation method for bacteriological diagnosis and on fermentation tests, as control of the purity of carbohydrate preparations.**] *Meddelelser f. d. Kgl. Vet.- og Landbohøjsk. Serumlab. Kjøben.*, 1920, No. **68.**

Although the estimation of gas production by bacteria in Durham's tubes is technically excellent, the author has worked out a micro-test solely in order to reduce as much as possible the consumption and cost of some of the rarer substances used, and in this communication he shows that his method with inverted tubes works perfectly with quantities of half a milligramme of the carbohydrate per test, thus giving 2,000 possible estimations per gramme—a quantity 40 times less than that required in the ordinary way. Glass tubing 1·5 mm. in diameter is used, and one end is slightly constricted in the flame. The other end is furnished with a cotton plug armed with an insect needle for convenience of handling, or plugged in the ordinary way. The tubes are about 100 mm. long. After dry sterilization a quantity of broth is sucked in. This is easily controlled by measuring the length of the column of the fluid, 56·5 mm. corresponding to 0·1 c.c. in a 1·5 mm. tube. After the end of the tube is removed from the broth it is sealed, care being taken not to burn the contents, which can be dislodged to the closed end by tapping gently on a table. All air-bubbles should be made to burst before the tubes are sterilized, during which process they should be protected from moisture by cotton-wool or filter-paper. Inoculations are made with a fine wire or a capillary tube, the tubes being closed by the armed plugs above mentioned or by means of an outside cotton-wool closure. This is applied by taking a series of tubes (4 cm. long and 5 mm. diameter) containing very loosely-packed cotton wool into which the microculture is *inverted*.

With these minute quantities the author demonstrated the occurrence of mutations in arabinose solutions by a *B. paracoli* and in rhamnose by an 'Isocoli' strain. In one experiment the percentage of tubes showing mutations was 95 in an ordinary quantity of medium and 85 in the microquantity. The second part of the paper deals with the very important question of the value of bacterial fermentation tests as a control of the chemical purity of carbohydrate preparations. Five tests of this nature are described in detail. In the first the question whether a solution of melibiose was contaminated with fructose was answered in the negative by the fact that *B. morgan*, which ferments fructose but not melibiose, gave a negative reaction, whereas *B. paratyphosus* B, which ferments both fructose and melibiose, gave a fermentation with the sugar under examination. In another experiment of a similar character it was proved that a sample of sorbitol also contained glucose as an impurity. The smallest quantity of xylose which can be recognized by fermentation tests was investigated and corresponded to a percentage of 0·025 (1 mg. in 4 c.c. of bouillon) in ordinary test tubes and 0·25 decimilligrammes in 0·1 c.c. in the author's micro-test tubes. Attempts were made to estimate the impurities (xylose and galactose) quantitatively in an arabinose preparation, and of the former more than 10 per cent. was found, while of the galactose the quantity was considerably less. In a commercial sample of arabinose an impurity (galactose ?) was found in 1–2 per cent. solutions, but not in a 0·5 per cent. solution. Glucose (?) was also encountered in a preparation of rhamnose. The cultures employed by the author for making these determinations are given; they came from the large collection of Prof. C. O. Jensen in Copenhagen. In conclusion, the author emphasizes the importance of working with pure substances in fermentation tests of a delicate character, and appeals for a collaboration with special chemical institutes where the rarer forms of carbohydrates, &c., are made, and he has authority to place the assistance of the serum laboratory of the Royal Veterinary and Agricultural College of Copenhagen, with its great collection of cultures, at the disposal of manufacturers of sugars and allied substances. W. B.

JACOBY, FRITZ. Die Bedeutung der Azidität der Ruhrstühle für die bakteriologische Ruhrdiagnose. [**The importance of acidity of dysenteric stools in the bacteriological diagnosis of dysentery.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 1.

This is a study of the changes in acidity of dysenteric stools, especially with reference to the diagnosis of dysentery. The stools in question, to the number of 150, were examined at stated intervals by means of decinormal acid or alkali with phenolphthalein as an indicator, the different faecal samples being classified according to their naked-eye appearance and consistence. Curves were constructed showing the changes in reaction. The author believes that the acid reaction of a dysenteric stool is independent of dysentery bacilli. The reaction in fact depends on such factors as the consistence of the stool, the nature of the pathological products in the stool, and the temperature at which it is kept. From the fact that with increasing acidity of the stool it becomes more and more difficult to find dysentery bacilli by bacteriological methods it would seem that the danger of transmitting the disease from acidified faecal matter cannot be very great, although Shiga and Flexner dysentery bacilli are not equally sensitive to acids. W. B.

WAGNER, G. Beiträge zur Epidemiologie und Bakteriologie des Paratyphus A sowie Untersuchungen über das Gärvermögen der Typhoideen. [**Contributions to the epidemiology and bacteriology of paratyphoid A, including investigations into the fermentative powers of the typhoideae.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 37.

This paper deals especially with a culture of *B. paratyphosus* A, which was isolated along with a culture of *B. typhosus* from the pus of an abscess over the sternum in a sailor. The origin of the infection was not ascertained.

Of interest is the fact that certain of the colonies of the paratyphoid culture were sensitive to sugars and showed forms similar to those described by von Lingelsheim as 'Q' types. The author tested various members of the typhoid-enteritis-coli group on a large number of sugars, alcohols, and other substances. Among the latter he found that formic, succinic, acetylformic, glyceric, tartaric, and citric acids in the form of salts were fermented by certain of the typhoid-coli group especially by *B. paratyphosus* A and *B. enteritidis*, Gärtner. W. B.

Feiler, M. Zur Biologie des Typhusbacillus. Ein Beitrag zur Wirkungsweise der Disinfektionsmittel und des Hungers auf Bakterien. [**The biology of the typhoid bacillus; a contribution to the mode of action of disinfectants and starvation on bacteria.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, **29** Orig., 303.

This is mainly a study of the effects on the *B. typhosus* and *B. paratyphosus* B of growth in media containing carbolic acid and on media containing a reduced quantity of nutritive substances so as to induce a condition of starvation. For the first, 2 c.c. of a 5 per cent. solution of phenol was added to every 100 c.c. of nutrient agar, the second medium being a 2 per cent. agar made up with equal parts of tap and distilled water. To 90 c.c. of this, 10 per cent. bouillon is added. As a result of growth on the carbolized medium the typhoid bacillus loses its flagella and with this disappears one of the agglutinogenic groups. The author considers that there are two agglutinogenic groups, the one belonging to the endoplasm the other to the ectoplasmic ciliary apparatus. The agglutinogens correspond to two agglutinins in the serum of immunized animals. If an animal is immunized with a culture grown on carbolic agar the agglutinin produced has been developed from the agglutinogen which has not been injured by the carbolic acid. In general a carbolized strain is agglutinated by immune serum evoked by ordinary typhoid cultures, more markedly and in a higher titre than ordinary strains of the same opacity in suspension.

If to immune serum produced from carbolized strains ordinary unmodified typhoid bacilli be added, it is found that the latter have absorbed all the agglutinins. Carbolized strains absorb all the agglutinins from the homologous serum, but absorb only part of the agglutinin from a serum produced by the injection of non-carbolized typhoid bacilli. This apparently shows that the culture of the microbe in carbolic agar has robbed it of part of its agglutinogenic properties. Races of typhoid grown on starvation media behave like the original strain. The carbolized strain was found to be as sensitive to the bactericidal action of normal human or immune animal serum as the original unmodified strain. It also possessed the same resistance, as original strains, towards physical and chemical noxae. The virulence for guinea-pigs was also found to be unaltered. Culture of the original strain in starvation media produced approximately the same results as growth in 1 per thousand carbolic acid, although in general the morphological and agglutinogenic characters were not so profoundly modified. A return to normal optimal conditions of medium caused both modified forms to assume their original condition in every respect. A similar state of affairs was produced with *B. paratyphosus* B cultures. The common agglutinogens of *B. typhosus* and *B. paratyphosus* B were not destroyed by growth in carbolic agar, from which the author infers that they originate in the endoplasmic rather than in the ectoplasmic apparatus.

W. B.

Weil, E. u. Felix, A. Ueber den Doppeltypus der Rezeptoren in der Typhus-Paratyphus-Gruppe. [**The double type of receptor in the typhoid-paratyphoid group.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 24.

In this study the discoverers of the Weil-Felix reaction make a further application of the idea that certain bacteria have double receptors of an O and H class (see p. 83). Working with certain bacteria of the paratyphoid-enteritis group they found that a bacillus allied to *B. Voldagsen*, and designated by them in this paper as paratyphoid β, was isolated from cases of fever in Wolhynia. The serum from three patients in Wolhynia agglutinated the homologous strains in the finely floccular manner characteristic of the O types of Proteus X 19. The sera, however, agglutinates paratyphoid B in the ordinary coarse floccular form. From these observations the authors began a long investigation on the receptors of the typhoid-paratyphoid-enteritis group of bacteria and found in fact that paratyphoid β has a double type. They utilize the fact that the thermo-stability of the two receptor types is different, for differentiating them still more exactly. Cultures in which the H receptors have been destroyed at 100° C. give only fine agglutination when mixed with the serum of an animal treated with heated cultures. The agglutination is of the fine floccular type. The proof of the double receptor type in paratyphoid A and B bacilli was more difficult, but was achieved by using the cloudy fluid which remains above the flocculi obtained by mixing the culture with agglutinating serum. Similar results were obtained with *B. enteritidis*, Gärtner. The stable O receptors were found to be very resistant towards high temperatures, alcohol, hydrochloric acid, sodium hydrate, or carbolic acid. Injections of the bacteria heated to 100° C. evoked agglutinins which produced almost entirely the fine type of flocculation. The cultivation of O types in the paratyphoid group was, however, not successful. A prolonged series of observations led the authors to the view that the co-agglutination often seen with sera of the paratyphoid group is due to the existence of one type of receptors which is common to several bacteria and is often of the fine floccular type. With regard to the significance of the two types of agglutination as a method of differentiation, Proteus and the typhoid-paratyphoid group behave in an opposite manner, for with Proteus it is the thermostable, fine floccular O receptors which are specific, whereas in the typhoid group it is the H thermolabile receptors which determine the mark of specificity. Paratyphoid β occupies an intermediate position.

W. B.

Schierge, M. Ueber die Beziehungen der Typhusagglutinine zu den Eiweisskörpern des Serums. [**On the relation of typhoid-agglutinins to the proteins of serum.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 527.

Ever since Brodie (1897) demonstrated that diphtheria antitoxin was completely precipitated from a solution by any means which removed the globulins there has been a general belief that in some way the antitoxin is

related to the globulin content, although workers have not been in agreement whether the relation was to the 'euglobulin' or the 'pseudo-globulin' fraction. The present author has investigated the relations of antityphoid agglutinins to the proteins of the serum, and experimented with ammonium sulphate as well as precipitation by means of carbon dioxide. The euglobulin solution was found to be strongly agglutinating although not in the same titre as the original serum. In order to determine the relation existing between the serum proteins and agglutinins in the normal condition as they exist in the serum he employed kaolin or dialysed iron (*Ferrum oxydat. dialysat.*), as recommended by Michaelis and Rona, and found that the agglutinins are not related to any particular fraction. Under certain circumstances the serum-albumin may contain the agglutinins, and he concludes that the process is a physical one of adsorption of the agglutinins, the difference in agglutinin content of the various fractions being due to different adsorptive capacities. The partition of agglutinins between the albumin and globulin fractions cannot be changed by the artificial addition of albumin, the original adsorptive capacity and fixation being unalterable.
W. B.

Jötten, K. W. Die Verwendung neutralisierter Antiformin-Bakterienauflösungen zur Gewinnung hochwertiger agglutinierender Ruhrimmunsera. [**On the use of neutralized antiformin solutions of bacteria for the production of high-grade agglutinating dysentery sera.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 267.

On account of the toxic character of antigens made from dysentery bacilli the author made a series of experiments and found that concentrations of antiformin down to 0·1 per cent., and subsequently neutralized and dechlorinated, killed the bacilli in 10 seconds and detoxicated them. By means of the following technique it was possible to obtain a non-toxic antigen which nevertheless evoked the production of high-grade agglutinating sera in rabbits. The culture of Shiga's bacillus grown for 24 hours on an agar plate was mixed with 2 c.c. of a 4 per cent. antiformin solution. After 1 minute it was neutralized by 10 per cent. H_2SO_4 and dechlorinated by a 10 per cent. solution of sodium sulphite (Na_2SO_3). The whole of such a solution could be injected into rabbits without ill effects, while in 9 days the agglutinating titre of the serum acted in a dilution of 1 : 10,000. Similar favourable results were obtained with Y and Schmitz's bacilli. W. B.

Šikl, H. Bakteriologische Untersuchungen am pathol.-anatomischen Material von Bazillenruhr. [**Bacteriological investigations on pathological-anatomical dysenteric material.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 337.

The author had exceptional opportunities of studying post-mortem material obtained from cases of dysentery in a large military hospital at Pardubitz (Bohemia). Bacteriological investigations were conducted in 96 cases, dysentery bacilli being found in 52. Of these only 5 were *B. shiga*. Almost all the cases investigated by the author were chronic, and the only selection was governed by external circumstances. The patients had been invalided from the most diverse parts of the front, and were not necessarily suffering from clinical dysentery, although dysentery bacilli were isolated from the mucous membrane of the bowel. Chronic dysentery was shown anatomically to be of a recurrent character. For the continuity of the dysenteric process, mucous cysts and submucous abscesses of the wall of the large intestine appeared to be of great importance. Diarrhoea in the course of malaria, tuberculosis, and septic processes was often proved by the author to be dysenteric in character. W. B.

Bitter, L. Massenerkrankung an Gastroenteritis nach dem Genuss von geräucherten Makrelen bedingt durch das Bacterium enteritidis Breslau. [**Epidemic of gastro-enteritis following the consumption of smoked mackerel and caused by *B. enteritidis*, Breslau.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 387.

Epidemics of gastro-enteritis following the consumption of fish have been rarely recorded. In the present epidemic over 300 persons in Kiel were seized with acute symptoms after having partaken of some consignments of smoked mackerel. In addition, there were cases in other parts of Germany to which some of the mackerel had been distributed. The fish in question were dispatched, fresh and packed in ice, from Skagen (Denmark), and were afterwards smoked in several factories in Kiel, and then placed on the market. Not all the mackerel proved poisonous, and the appearance and taste of those that were infective were perfect. The symptoms were vomiting, fever, and severe diarrhoea; at least three old people died. In the stools and urine of a large number of affected persons during life, and in the blood and viscera of the three fatal cases, large numbers of bacilli of the enteritidis group were found without difficulty. An examination of the cultures and their agglutinating reactions led the author to the conclusion that the bacillus was identical with that isolated many years ago by Kaensche in Breslau, and generally placed in the aertryck group agglutinogenically. With a Gärtner serum agglutination was slight, whereas with 'Breslau' serum the microbe isolated was agglutinated to titre. With a paratyphoid B serum $\frac{1}{5}$ of the agglutination titre was reached. Mice fed on bread soaked with living cultures invariably succumbed with a septicaemic invasion in 8 days, and similar results were obtained with infusions from the incriminated mackerel. After analysing the epidemics of poisoning from fish the author discusses the probable source of the infection without arriving at any certain conclusion. W. B.

Bruns, Hayo u. **Gasters.** Paratyphusepidemie in einer Hammelherde; dadurch bedingte Massenerkrankungen an Fleischvergiftung in Überruhr (Landkreis Essen). [**Paratyphoid epizootic in a flock of sheep with consequent epidemic of meat poisoning in Überruhr (Essen district).**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 263.

This is an account of a very large epidemic of paratyphoid fever in Überruhr (Essen district), a place of over 4,000 inhabitants, of which about half were affected. There were 40 to 50 severe cases and at least 3, possibly 4, deaths. The origin of the epidemic was traced with certainty to the flesh of sheep which had to be slaughtered on account of illness originally alleged by veterinary surgeons to be due to the excessive consumption of salt. The carcases were officially passed as healthy, the meat being distributed to the inhabitants on June 28, 1919. Within a few hours large numbers fell ill with fever, vomiting, colic, severe diarrhoea, and cramps in the legs. By July 4, *Bacillus paratyphosus* B had been isolated in large numbers from the incriminated flesh, although when inspected it appeared to be perfectly fit for human consumption. In three elderly people, who succumbed to the disease, paratyphoid bacilli were easily found both in the bowels and in the viscera and glands. A fourth fatal case was not so certain. It was that of a child three months old who, however, had suckled its mother, then suffering from paratyphoid fever. The bacilli found in the human cases were identical with those isolated from the flesh of the affected sheep. These animals belonged to a flock numbering about 300, of which, within four or five weeks, 160 died or had to be slaughtered on account of a disease which was associated with fever, wasting, weakness, and stinking diarrhoea. There was reason, however, to believe that the survivors of the flock had also been extensively infected. Autopsies made on manifestly diseased animals revealed the signs of acute enteritis, paratyphoid bacilli being easily isolated from the viscera. The source of the epizootic was not definitely cleared up. It was ascertained that the flock had been brought from Bavaria on June 23/24 and were several days on the way packed in railway vans under very defective sanitary conditions. Within a few days of their arrival in Überruhr, where they were closely confined in pens, they began to suffer and some had to be destroyed. The important question whether, in the sheep, the disease was an enteritis or a general sepsis could not be determined, because before the investigations on this point were undertaken the epizootic had largely subsided. Paratyphoid bacilli were not cultivated from the blood during life. The recovery, however, of bacilli from the flesh indicated a general infection rather than a local enteritis. An interesting aspect of this report is the demonstration that the sheep actually suffered from the same disease which affected the human cases. It has often been believed that, in cases of meat poisoning, the flesh of the animal was not in itself infective but became so from human or other contamination after the animal had been slaughtered. A further item of great rarity is that the flesh of sheep caused paratyphoid in man. Epidemics of meat poisoning from mutton are rare. In an analysis of the sources of epidemics of meat poisoning Schneidemühl concluded that in point of frequency cow's flesh came first with 62 per cent., calves' flesh 21 per cent., ox flesh 5 per cent., pig's flesh 5 per cent., horseflesh 3 per cent, sheep's flesh 0 per cent. The few experiments that have been made also indicate that sheep cannot be readily infected with paratyphoid bacilli unless massive doses of cultures are administered to them. W. B.

Lorenz, F. Eine Dysenterie-Y-Milchepidemie. [**A milk-borne epidemic of dysentery Y.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 423.

In the course of 24 hours 150 children in the Hamburg Orphan Asylum, which contained 1,500 inmates, were seized with diarrhoea, vomiting, and fever. In some cases the disease was severe, and in five cases fatal. Inquiry rendered it probable that the source of the trouble was milk, as it had been drunk only by those who were attacked. Within a day or two *B. dysenteriae* Y was isolated from the milk without difficulty and also from many of the patients. The milk, which came from an unimpeachable source, had been delivered at the home the day before the outbreak and had at once been boiled and placed in the larder near the kitchen. The same milk had been delivered to other institutions without ill effect. It was therefore clear that it must have been infected in the orphanage home after sterilization. All the persons occupied in the kitchen were examined, but with a negative result. It was ascertained, however, that on the day before the epidemic began a female servant in the kitchen had suffered from a dysenteric-like condition, but had actually left before the disease started among the children. It was not possible to examine this woman until three weeks later, and by that time no dysentery bacilli could be recovered from her faeces. Her occupation in the kitchen and her intestinal trouble rendered it exceedingly probable that the disease had emanated from her. In two of the fatal cases the autopsy showed cloudy swelling of the kidney, and in one the rare complication of myocarditis referable to dysentery toxin.

The dysentery Y cultures isolated from milk were typical biologically and were agglutinated in high dilutions by a Y serum and to a less extent in Flexner serum. The same was true, with variations, of the strains recovered from the stools. The infected milk was supplied on Aug. 28, the disease breaking out in the night Aug. 28/29. The stools of two patients examined on Aug. 30 were both negative, but by the following day dysentery bacilli were recovered in 13 out of 17 specimens tested (76·5 per cent.), while on the next day again the positive cases numbered 8 of 15 examined (53·3 per cent.). On subsequent days the percentage of positive results diminished rapidly. Within five days of the date on which the infected milk was drunk, three patients gave positive agglutination results in the serum. Experiments on animals led to the belief that the Y strains isolated were not unusually infective or toxic. The author believes, and brings experiments to show, that in all probability the destruction by sterilization of the bacteria in the original milk rendered the latter an admirable medium for the growth of the dysentery bacilli, which gained access to the milk in large quantities from a female who was most probably a dysentery carrier.

The investigation was carried out in the Municipal Hygienic Institute in Hamburg under the direction of Prof. W. Dunbar. W. B.

Weil, E. u. Felix, A. Weitere Untersuchungen über das Wesen der Fleckfieberagglutination. [**Further researches on the nature of typhus fever agglutination.**] *Wien. klin. Wchnschr.*, 1917, **30**, 1509.

Although this paper was published in 1917 it is abstracted here as it contains certain facts which have been the subject of much subsequent investigation which is difficult to follow in the absence of the original publication. Weil and Felix were the first to point out (*Wien. klin. Wchnschr.*, 1917, **30**, 393) that the agglutinating effect of the serum of typhus patients, on Proteus X 19 differs from that of rabbits or human beings inoculated with cultures of the same Proteus X 19. Immune serum, made by inoculating rabbits with X 19 agglutinates not only the homologous strain but also ordinary saprophytic Proteus bacteria, while typhus serum does not agglutinate ordinary Proteus strains more than does normal serum. In the present communication the authors assume the existence of two types of receptors in X 19 strains, viz. a 'specific' receptor and a 'substance' receptor, the latter corresponding to the receptors of saprophytic Proteus strains. In emulsions made with X 19 cultures typhus serum produces a fine uniform flocculence, whereas the serum of rabbits injected with X 19 cultures produces coarse unequal flocculi, an appearance which is very easily recognized. On examining, more attentively, some old cultures of X 2 and X 19 on agar plates they found some colonies which failed to show the characteristic filmy (hauchförmige) formation so frequently seen in ordinary cultures of Proteus. These colonies were small at first and even later showed no progressive growth. The authors distinguish them as 'O' colonies (O = ohne) and contrast them with 'H' (H = Hauch) colonies of saprophytic Proteus cultures. The O colonies alone are specifically agglutinated by typhus serum. Immune serum made from pure H forms induces a coarse agglutination, whereas sera made with O forms induces fine flocculi in the homologous cultures. Absorption experiments showed that the O forms possessed only one type of receptor—the specific one—whereas the H strains have two types of receptors—the specific one and the 'substance' receptor. The agglutinins which act on the O receptors are not so thermostable as those of H cultures. W. B.

Börnstein, P. Ueber den Bau des Rezeptorenapparates der Proteus-X-Bazillen. [**On the structure of the receptor apparatus of Proteus X bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1920, **90**, 206.

It was proved by Weil and Felix, and their statements were confirmed by others, that the agglutinins for Proteus X 19 in the serum of typhus patients differ from the agglutinins evoked in the body of human beings or rabbits inoculated with cultures of Proteus X 19. Friedberger, however, with an inverted modification of Castellani's absorption method came to the conclusion that there was no difference in the two types of sera, and he regarded the X 19 bacillus as the dominant cause of exanthematic typhus. Friedberger's method consisted in saturating X 19 bacilli with homologous rabbit serum and thereafter saturating it with typhus patient's serum. In cross-experiments X 19 was first saturated with patient's serum and then with immune rabbit's serum. In both series the saturation with the first serum sufficed to prevent a saturation with the second serum, and thus he concluded that the agglutinins in the two sera were identical and had originated from the same microbe, viz. bacillus X 19. The present author has worked along the same lines with results which differ from those of Friedberger. He comes to the conclusion that X 19 bacilli have two definite types of receptors, the one (orthoreceptors) common to Proteus bacilli in general, the other (parareceptors) which are specific for typhus fever. Saturation of the one group with agglutinin removes the capability of combining with agglutinin of the other group more or less. W. B.

Michaelis, Wolfgang. Der Einfluss des Nährbodens auf die Weil-Felixsche Reaktion. [**The influence of the medium on the Weil-Felix reaction.**] *Deutsche med. Wchnschr.*, 1920, **46**, 619.

The author found that Proteus X 19 grown in glucose-free media was agglutinated by immune rabbit serum only when the latter was present in strong concentration. The addition of glucose increased agglutination and ultimately caused it to take place spontaneously. Solutions of lactose had no such effect. W. B.

Schiff, F. Zur Theorie der Weil-Felixschen Reaktion. [**The theory of the Weil-Felix reaction.**] *Ztschr. f. Immunitätsforsch.*, 1920, Orig. **29**, 11.

Without introducing any original data the author discusses in a lucid manner the various theories which have been advanced to explain the Weil-

Felix reaction and concludes, as Weil and Felix originally did, that the reaction is a specific agglutination of a specific form of Proteus, viz. that called X 19. W. B.

Bach, F. W. Untersuchungen über die Säureflockung von Proteus-Stämmen. [**Investigations on the acid agglutination of Proteus strains.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1920, Orig. **84**, 265.

This is a study of acid agglutination with 8 specific X strains from typhus patients and 14 non-specific, i. e. ordinary, strains of Proteus. Following Beniasch (*Ztschr. f. Immunitätsforsch.* 1912, Orig. **12**, 268) the agglutination was determined with a series of nine mixtures of lactic acid and sodium lactate, the ratio of lactic acid (decinormal) to sodium lactate (decinormal) in the nine tubes being 1:8, 1:4, 1:2, 1:1, 2:1, 4:1, 8:1, 16:1, and 32:1. Both the H and O types of Weil and Felix were tested. The H types of specific Proteus cultures showed great uniformity in acid agglutination, whereas the H types of ordinary Proteus varied greatly both with respect to the X 19 H strains and among each other. There was also great variability among the O strains whether derived spontaneously in Proteus X cultures or artificially produced by growing ordinary Proteus strains in carbolized media. The type of acid agglutination in O cultures was also very different from that witnessed in H cultures. Serum and acid agglutination may run parallel but not necessarily so. The author thinks that acid agglutination cannot be employed for the differentiation of typhus from ordinary Proteus strains. W. B.

Friedberger, E. Ueber die sogenannte Fleckfieberinfektion des Meerschweinchens nach Uebertragung von menschlichem Fleckfieberblut. [**On the so-called typhus infection of guinea-pigs, following the inoculation of blood from human cases of typhus.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 125.

This is an attempt to minimize the importance of the experimental work which has been done on the transmission of typhus fever to guinea-pigs. The author has already expressed his conviction that the Weil-Felix Proteus X 19 stands in causal relation to the disease. In the present communication he describes the effects observed in guinea-pigs injected with the blood of typhus patients at the beginning or height of the disease. A large number of observations are detailed on the changes in temperature and weight of the inoculated animals. The author was unable to produce any marked clinical condition which could be identified with typhus fever. In comparison with the changes in temperature and weight there was no marked or constant difference between animals injected with typhus blood or with the blood of healthy persons. A transitory rise in temperature may occur in both series either soon after the inoculation or at an interval of one month or more. W. B.

Hahn, Martin u. **Neu, H.** Ueber das Verhalten der Antikörper des Normalserums bei täglich wiederholter Blutentziehung. [**On the behaviour of the antibodies of normal serum towards daily repeated withdrawals of blood.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 349.

In 1917 Hahn and Langer, in a paper which was reviewed in the *Medical Supplement* (1918, **1**, 147), tested the effect of daily repeated bleeding, on rabbits immunized with bacilli of the typhoid group, for the production of agglutinins, and with sheep's blood for the production of haemolysins and precipitins. Twenty c.c. of blood were withdrawn daily from the ear vein, the venesections commencing when the curve of the antibody content began to fall. In every instance an extraordinary increase in the agglutination titre was said to have been observed, actually, in one case, up to 1:128,000,000. It may be said that Landau, repeating this work, was unable to confirm these statements. In the present publication Hahn and Neu have studied the effects of repeated bleeding on the serum of normal rabbits when its bactericidal action for *B. typhosus* and *Staphylococcus* or its haemolytic action on sheeps' corpuscles was examined. The results showed that daily venesections of quantities of 20 c.c. caused a definite increase in bacteriolysins, but had no effect in raising the haemolytic titre. The increase in bactericidal power was not altered when the serum was heated for half an hour at 56° C. and began to disappear only when a temp. of 60° was maintained for thirty minutes. The authors attribute the increased bacteriolysis to the presence of so-called 'leukines', which are said by Schneider to be relatively thermostable, and are derived from the leucocytes. W. B.

Breinl, F. Ueber die Agglutinine des normalen Rinderserums. [**On the agglutinins of normal ox serum.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 491.

Following up the work of Weil and Felix on the two types of agglutinogenic receptors in Proteus X 19 and other bacteria (vide pp. 79 and 83) the author made experiments to determine whether the same holds good with respect to normal ox serum which contains agglutinins for certain bacteria. The author employed emulsions of Proteus of the 'O' and 'H' types as well as *B. typhosus*, *B. paratyphosus* A and B, and *B. enteritidis*, Gärtner, and found in fact that there are two agglutinating types of receptors, as could be demonstrated by absorption experiments. For example, a culture on agar was suspended in saline and thoroughly centrifuged. The supernatant liquid was removed by a pipette and the deposit incorporated with normal ox serum and combination was allowed to take place for an hour in the thermostat, after which the suspension was centrifuged and the fluid tested. Working with Proteus the author found both coarse and fine agglutination in ordinary cultures, whereas with 'O' strains the fine agglutinins were removed while the coarse agglutinins remained. Similar results were obtained with members of the typhoid-paratyphoid group. The experiments indicate that the agglutinating mechanism in normal ox serum is more complicated than has hitherto been supposed. W. B.

Cori, K. und **Radnitz, G.** Ueber den Gehalt des menschlichen Blutserums an Komplement und Normalamboceptor für Hammelblutkörperchen. [**On the content in human blood-serum of complement and amboceptor for sheep's corpuscles.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1920, Orig. **29**, 445.

The author has tested the content of complement and amboceptor of human blood-serum when tested on sheep's erythrocytes. Eighty-four examinations on 52 persons were made, the majority being patients suffering from a great variety of different morbid conditions including typhoid fever, pneumonia, influenza, anaemias of diverse origin, polycythaemia, myeloid leukaemia, nephritis, &c. He found that the complement content of the serum of these persons varied between 0·25 and 0·015, the commonest value being 0·06. The amboceptor value varied between 0·25 and 0·0019, and was most frequently 0·03. Of 16 febrile cases examined, 10 showed increased complement content, 3 average, and 3 lowered complement content. In myeloid leukaemia there is a fall of complement and amboceptor 3 to 7 days after the application of X-rays. The complement content is lowered in syphilis. There appears to be no relation between the protein content of the serum and the complement or amboceptor titre.

W. B.

BIOCHEMISTRY

Pugliese, A. Le processus de la croissance dans l'hypofonction d'une ou plusieurs glandes endocrines, provoquée expérimentalement chez les chats et les chiens tout jeunes. [**The effect on development of hypofunction of one or more endocrine glands brought about experimentally in very young cats and dogs.**] *Arch. ital. de biol.*, 1920, **70**, 1.

In adult or nearly full-grown dogs or cats, simultaneous extirpation of one suprarenal capsule and one lobe of the thyroid, whether or not combined with splenectomy, does not give rise to any bad results. Animals so treated remained in good health and were capable of producing and bringing up young.

In young dogs and cats, unilateral thyro-parathyroidectomy alone resulted in an increase of body weight which was diminished by extirpation of the suprarenal. Very young animals generally did not survive the operation for more than 80 to 104 days. They showed an enormous reduction of body fat and considerable modification in the composition of the skeleton.

After the removal of one suprarenal capsule and unilateral extirpation of the thyroid, the remaining suprarenal and thyroid tissue showed compensatory hypertrophy.

Unlike young cats, very young dogs survived the operation, but grew less rapidly than the controls, and showed less general resistance to fatigue and other influences. The bones of such dogs were smaller and thinner than those of normal animals of the same age, but no definite change in their composition was determined. Evidence of compensatory hypertrophy was not so evident in dogs as in cats. Great alterations in weight were apparent in some of the internal organs, the liver being chiefly affected; the muscles apparently underwent no change.

H. M.

Wishart, G. M. **The effect of injection of guanidin on the creatin content of muscle.** *J. Physiol.*, 1920, **53**, 440.

The creatin content of the muscles is increased by the intravenous or subcutaneous administration of inorganic salts of guanidin, the increase varying with the dose. This increase is not an apparent one depending on changes in water content, nor is it altogether, if at all, due to the accompanying alkalosis.

H. M.

Krogh, A. and **Lindhard, J. The changes in respiration at the transition from work to rest.** *J. Physiol.*, 1920, **53**, 431.

The changes in respiration induced by muscular work only gradually return to normal level after the work is stopped. The oxygen deficit caused by the lagging behind of the oxygen during the very early stages of work is not compensated during work. After the cessation of heavy work, the respiratory quotient rises, often far above unity, and this increase is continued for about one and a half minutes. This increase may be due to washing out of CO_2 by fixed acids in the blood; it is followed by a definite decrease, sometimes to subnormal values. H. M.

Cushny, A. R. The colloid-free filtrate of serum. *J. Physiol.*, 1920, **53**, 391.

When serum is filtered through a collodion membrane which retains the colloids, the filtrate contains most of the non-colloidal bodies such as salts, sugar, and urea, in the same proportions as in the original serum. The only exceptions to this rule are calcium and possibly magnesium, which occur in the filtrate in a lower concentration than exists in the serum. This result suggests that all the non-colloidal constituents, with the exception of calcium and magnesium, exist in simple solution in the serum, while part of the calcium and magnesium is probably in combination with the protein. The fact that calcium is partly excreted by the intestinal epithelium may be connected with this combination in the serum. No such combinations as have been suggested by the term 'ion-protein' occur in blood-plasma, and from this it follows that proteins are incapable of expelling the CO_2 from bicarbonates. If filtration occurs in the kidney glomerulus, the filtrate must be practically identical with that obtained when serum is filtered through a suitable collodion membrane. H. M.

Krogh, A. Studies on the capillariomotor mechanism. I. The reaction to stimuli and the innervation of the blood-vessels in the tongue of the frog. *J. Physiol.*, 1920, **53**, 399.

The arterial pressure is unable to dilate the capillaries to any appreciable extent or open them up when they are tonically contracted. When, however, relaxation is induced as the result of weak mechanical or chemical stimuli, the venous pressure may be sufficient to fill them. The state of filling of the capillary vessels is, therefore, not determined by the arterial blood-pressure, but depends on the degree of tonus or relaxation of the capillary wall.

Both capillaries and arteries may be dilated by the local application of mechanical, thermal, and chemical stimuli (weak acids, cocaine, adrenalin, &c.). Urethane dilates the capillaries but does not affect arteries. Cocaine abolishes the reaction of the vessels to local stimulation. The same result follows after section and subsequent degeneration of the nerves. The capillary tonus does not appear to be of nervous origin, at least to any great extent, but depends upon the supply of blood. The substance in the blood responsible for this tonic action is unknown, but it is certainly not oxygen. H. M.

Burns, D. and **Watson, A. The effect of thyro-parathyroidectomy on the heart and circulation. Part II. Action of guanidin on the heart of the frog.** *J. Physiol.*, 1920, **53**, 386.

Guanidin salts in concentration of 0·25 to 1·7 per cent. produce, at first, acceleration of the cardiac rate, probably as the result of stimulation of the accelerator nerves of the heart. This acceleration is soon followed by prolonged and marked retardation of the heart-beat caused by (1) stimulation of the vago-cardiac nerves and (2) pronounced vasoconstriction with reflex inhibition. By the use of atropin and nicotin it was shown that guanidin acts on the sympathetic neurons. H. M.

Barcroft, J., Cooke, A., Hartridge, H., Parsons, T. R., and **Parsons, W. The flow of oxygen through the pulmonary epithelium.** *J. Physiol.*, 1920, **53**, 450.

Under a condition of anoxaemia caused by living for six days in an atmosphere in which the partial pressure of oxygen fell to 84 mm., analyses of the alveolar air and arterial blood in man showed that the arterial blood *in vivo* contained less oxygen, both during rest and work, than did samples of the same blood exposed to alveolar air *in vitro* at body temperature. The quotient of oxygen consumption and difference in oxygen pressure yielded during work a diffusion constant of about 100. There was no self-reduction of the blood sufficient to invalidate the determination of the percentage saturation of the blood taken directly from the radial artery. H. M.

Ciamician, G. and **Ravenna, C.** Action des enzymes végétaux sur quelques substances organiques. [**Action of vegetable enzymes on certain organic substances.**] *Arch. ital. de biol.*, 1920, **70**, 46.

A paper dealing with experiments on the oxidation enzymes of living and dead plants. Sodium benzoate injected into rice plants disappeared to a large extent with the formation of approximately equivalent amounts of acetic, formic, and propionic acids. H. M.

Krogh, A. and **Lindhard, J. The relative value of fat and carbohydrate as sources of muscular energy, with appendices on the correlation between standard metabolism and the respiratory quotient during rest and work.** *Biochem. J.*, 1920, **14**, 290.

One of the fundamental problems of nutrition is the question as to whether fats can be utilized as sources of energy with the same efficiency as carbohydrates. It has been presumed that certain reactions take place in the transformation of fats into energy which involve a loss of heat. This view has been confirmed by the results obtained by Fletcher, Hopkins, and Hill. Krogh and Lindhard have attempted to review the whole question, by a most careful study of the respiratory metabolism of individuals who were living on a minimum of protein and carrying on nutrition by the ingestion of carbohydrates or of fats. At a certain time a definite amount of work was done. The standard resting metabolism had been previously determined. Knowing the amount of work performed, and the respiratory exchange, it is possible to ascertain whether carbohydrate or fat is the more efficient. In a previous paper Krogh describes a gas-analysis apparatus of great accuracy which has been of assistance to him in deciding small differences in the respiratory exchange. About 220 determinations were made. All the series agree in showing that work is more economically done with carbohydrate. With carbohydrate a calorie of technical work can be performed by the katabolism of 4·1 cal., while the same amount of work requires 4·6 cal. of fat. Training tends to economy in utilization. It is noteworthy that when the subjects were tired they worked with greater difficulty on fats than on carbohydrates. The waste of energy when fats are utilized is estimated at 11·0 per cent. C. G. L. W.

Widmark, E. M. P. Studies in the acetone concentration in blood, urine, and alveolar air. II. The passage of acetone and aceto-acetic acid into the urine. *Biochem. J.*, 1920, **14,** 364.

Experiments were performed by the author on himself by taking known amounts of acetone by the stomach and estimating the acetone excreted in the urine and blood at fifteen-minute intervals. Estimations of the acetone concentration in blood and urine were made in a case of diabetes after the ingestion of water. The process by which the acetone reaches the bladder is one of diffusion. The concentration in blood and urine is therefore the same. Aceto-acetic acid is eliminated by a selective action of the kidneys and hence the concentration of the substance is greater in the urine than in the blood. C. G. L. W.

Höst, H. F. and Hatlehol, R. Blood-sugar concentration and blood-sugar methods. *J. Biol. Chem.*, 1920, **42,** 347.

The paper is a criticism of the various methods employed for analysis of the sugar in blood. Reducing methods are usually employed for the analysis of sugar in blood. The blood contains many other substances which reduce, besides glucose. Instances of these are fructose, ketones, uric acid, creatinin. Tho question as to how far these other substances may interfere with the estimation is a difficult one. Höst and Hagedorn have done a series of comparative experiments, using four different methods of analysis. The results came out as follows. For a number of analyses (about 20) in each case:

	Average Error	Greatest Error
Bang	2·7	8
Hagedorn	3·2	9
Benedict	3·0	7
Folin	4.5	10

Bang's and Hatlehol's methods and Hagedorn and Jensen's method give results which agree for normal individuals and for diabetics. Folin and Wu's method, as well as Myers and Bailey's modification of Benedict and Lewis's method, may give too high results, especially for diabetics with hyperglycaemia. By all methods, except that of Benedict, the value for the blood-sugar of normal individuals always came out as under 0·11 per cent.

R. A. P.

Reiman, C. K. and Minot, A. S. A method for manganese quantitation in biological material, together with data on the manganese content of human blood and tissues. *J. Biol. Chem.*, 1920, **42**, 329.

The authors have developed a method for analysing manganese in tissue extracts. They have found manganese in all tissues. The greatest amount was in the liver, averaging 0·170 mg. per 100 grm. of wet tissue.

R. A. P.

McEllroy, W. S. Method for the determination of methaemoglobin and haemoglobin in blood. *J. Biol. Chem.*, 1920, **42**, 297.

In this method, the total haemoglobin present (haemoglobin + methaemoglobin) is determined as methaemoglobin colorimetrically. The oxygen capacity then of the original sample measures the amount of haemoglobin present. The difference gives the amount of methaemoglobin.

R. A. P.

Lewis, H. B. The metabolism of sulphur. III. The relation between the cystin content of proteins and their efficiency in the maintenance of nitrogenous equilibrium in dogs. *J. Biol. Chem.*, 1920, **42**, 289.

Further proof is brought forward that the sulphur containing amino-acid cystin is essential for growth. Casein is low in cystin content. Serum albumin is high. When fed separately to dogs, nitrogenous equilibrium is maintained better on serum albumin than on casein. Casein, however, can be made as good as serum albumin by adding to it cystin.

R. A. P.

Williams, R. J. A quantitative method for the determination of vitamine. *J. Biol. Chem.*, 1920, **42**, 259.

By making use of the growth of yeast cells, it has been possible to measure the amount of vitamine in a given solution. The amount of growth of the yeast + vitamine is measured over and above that of a similar amount without vitamine. As the method is quantitative it is largely independent of the personal factor involved in the method of cell-counting.

R. A. P.

Fridericia, L. S. Exchange of chloride ions and of carbon dioxide between blood corpuscles and blood-plasma. *J. Biol. Chem.*, 1920, **42**, 245.

Hamburger originally made the observation that when pure carbon dioxide was led through a sample of blood, chlorides passed from the blood-plasma to the red blood corpuscles. This observation has been confirmed since.

The next question which naturally arises is whether a different amount of chlorides pass through for different amounts, or tensions, of carbon dioxide? Van Slyke and Cullen did some experiments upon this point. The author has repeated them in Copenhagen. He shows that as the tension of carbon dioxide rises, more chlorides pass into the corpuscles. This change in the distribution of chlorides is caused by the corpuscles. As the chlorides pass into the corpuscles, they cause an increase in the amount of available base (sodium) in the plasma, so that plasma with corpuscles can take up more CO_2 than plasma without corpuscles.

The corpuscles themselves alone also take up CO_2. For high tensions of CO_2, the reaction of the corpuscles is only slightly higher than that of the plasma. Hasselbach's interpretation of haemoglobin as an amphoteric electrolyte explains the increase of the CO_2 combining power of the corpuscles as well as the passage of chloride ions (and other ions) into the corpuscles. R. A. P.

Landsteiner, K. Spezifische Serumreaktionen mit einfach zusammengesetzten Substanzen von bekannter Konstitution (organische Säuren). XIV. Mitteilung über antigene und serologische Spezifität. [**Specific serum reactions with simple synthetic substances of known constitution (organic acids).**] *Biochem. Ztschr.*, 1920, **104**, 280.

This paper contains important new work upon the specificity of the precipitin reaction. When a foreign protein substance is injected into an animal the serum of that animal develops some body which is capable of precipitating the protein which has been injected. This reaction is called the 'precipitin' reaction. Up to the present time it has not been possible to relate this fact with chemical or physical views. There have been two classes of idea as to its action; the one that it is due to the interaction of certain colloids, and the other that it is really intimately connected with some chemical structure. The evidence brought forward by Landsteiner in this paper seems to decide in favour of the latter view. He has shown that one very specific reaction is closely concerned with the chemical structure of the substance employed.

In an earlier paper Landsteiner had shown that an azo-protein (made by combining protein with some chemical substance by the diazo reaction), when injected into an animal, evokes a substance in that animal's serum capable of precipitating the azo-protein. He has shown further that the specific group concerned is the azo one, because the protein used can be interchanged with any other intact one. When an azo-albumose is used instead of an azo-protein a much smaller precipitate is got. If a peptone or amino-acid (viz. the last products of protein breakdown) is used, no precipitate is formed. The formation of a *visible* precipitate requires, therefore, a combination of the azo group with some protein of a greater complexity than peptone.

In the extension of this work the author has made use of another reaction. The substance which evokes the reaction in the animal's serum (in this case the azo-protein) is known as the antigen. Antigen + immune serum in the right proportions give a visible precipitate. If excess of antigen is used, this precipitate is redissolved. This resolution of the precipitate by excess of antigen is again specific. Put briefly—

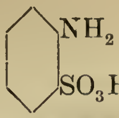
Antigen + immune serum gives a precipitate.

Antigen + *more antigen* + immune serum gives no precipitate.

The question which the author has put to himself is this: What simple chemical bodies will replace the '*more antigen*', and prevent the appearance of a precipitate in the same sense as the excess of antigen? If any simple substances do this, are they in any way specific?

When this matter was put to the test it was found that there was an almost exact chemical specificity for the simple substances that would produce this inhibitory reaction when added to the antigen.

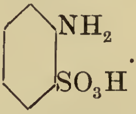
An illustration may perhaps make the meaning clear.

In one of the experiments, the substance  was linked by the author's diazo reaction to the protein from fowl's serum.

This azo-protein then formed the antigen.

The immune serum was prepared by injecting this antigen into rabbits, and so evoking the immune body in rabbit's serum.

When mixed together in the right proportions, the two substances, azo-protein and immune serum, produced a precipitate.

A series of compounds of the amino-acid, tyrosin, were then prepared. The above experiment with antigen and immune serum was then repeated with the following change. To the antigen was first added the tyrosin compound to be tested; and then the mixture so formed was added to the immune serum. It was observed that the only compound of tyrosin which prevented the precipitation was tyrosin + . In other words, it was possible to imitate the inhibitory action of excess *antigen* by adding to the mixture of antigen + immune serum the original chemical substance which evoked the precipitin reaction. It was later shown that the original substance alone or combined with tyrosin or other substances could produce the effect.

This case, quoted as an illustration, is only one of a large number of similar instances examined by Landsteiner, all of which show chemical specificity to a marked degree. It leads to the conclusion that the precipitin reaction itself will soon be put into terms of comparatively simple organic chemistry too. At any rate, we need no longer regard the whole matter as a colloid mystery incapable of solution upon the lines of ordinary chemical phenomena. The chemoceptor is some simple body, and depends for its action upon the reactions of ordinary structural chemistry. R. A. P.

HAGGARD, H. W. Haemato-respiratory functions. II. The Henderson-Morris method for determining the carbon dioxide in plasma and in whole blood. *J. Biol. Chem.*, 1920, **42**, 237.

The Henderson method of examining the CO_2 content of whole blood has been tested thoroughly and is found to be as easy as the estimation of plasma CO_2. The author of the paper claims that it is easier to apply to whole blood than the method of Van Slyke. R. A. P.

LARSEN, R. B. and **SECHER, K.** Sochanski's Methode til Adskillelse af Exsudater og Transsudater. [**Sochanski's test distinguishing between exudates and transudates.**] *Hosp. Tid.*, 1920, **63**, 273–8.

Larsen and Secher have carried out Sochanski's (*Wien. klin. Wchnschr.*, 1918, **32**, 493) test in 38 cases, details of which they publish in a table. They find that this test is of great value, and that it is far better than estimation of the nitrogen in a fluid in distinguishing between transudates and exudates. C. L.

Koritschoner, R. u. Morgenstern, G. Refraktometrische Untersuchungen über die Reaktionen zwischen isolierten Krebszellen und Blutserum (Freund-Kaminersche Reaktionen). [**Refractometer experiments on the reaction between isolated cancer cells and blood-serum (Freund-Kaminer Reaction.)**] *Biochem. Ztschr.*, 1920, **104**, 259.

The Freund and Kaminer reaction between serum and cancer cells can be measured with the refractometer. An increase of refractometer reading was given by 50 sera from carcinoma-free cases showing no fever. A decrease of refractometer reading was given by 15 sera from carcinoma-free cases showing fever. On the other hand, 30 non-febrile cancer cases showed a decrease of reading or no change.

The effects with prepared liver cases were the same for normal and carcinomatous individuals. R. A. P.

Krogh, A. u. Liljestrand, G. Eine Mikromethode zur Bestimmung der Kohlensäure des Blutes. [**A micro-method for the determination of the carbon dioxide of the blood.**] *Biochem. Ztschr.*, 1920, **104**, 300.

The authors describe a method of analysing the CO_2 content of 0·25–0·3 c.c. of blood saturated at artificial CO_2 tensions. This amount of blood suffices for a double estimation. The mean error is 0·5 per cent. of a volume of CO_2. R. A. P.

Schemensky, W. Untersuchungen über die Oberflächenspannung des Urins und ihre Anwendung auf die klinische Pathologie. [**Experiments upon the surface tension of urine and its application to clinical pathology.**] *Biochem. Ztschr.*, 1920, **105**, 229.

The author has used the measurement surface tension by the Traube stalagmometer as a diagnostic method for urines. By his method he claims to be able to pick out quickly certain cases of disease, such as bile in the urine and certain diseases of the kidney. He gives a great number of figures. R. A. P.

RADIOLOGY AND ELECTROLOGY

Radio-diagnosis

Bowman, W. B. Coccidioidal Granuloma. *Am. J. Roentgenol.*, 1919, **6**, 547.

Coccidioidal granuloma is a definite acute, subacute, or chronic disease due to an infection by a parasitic organism or mould-like growth, called by Ophüls the *Oidium coccidioides*. It is also called the California disease, as all the cases reported, except three, have either lived in or visited that State before contracting the disease. The *Oidium coccidioides* occurs as a spherical body varying from seven to thirty microns in diameter. It is an irregular protoplasmic body with a double contoured, highly refractile surrounding membrane or capsule, and it multiplies by sporulation. The mode of infection in the human is unknown. The pathology, both naked eye and histological, is practically identical with that of tuberculosis. A positive diagnosis can be made only on the finding of the organism in the pus or tissues. This is easily done by mixing a drop of pus with a drop of

10 per cent. sodium hydrate. After a few minutes, when the pus cells have been destroyed, the parasites, which are much more resistant, are easily found.

The author gives the case histories and X-ray findings in five cases which had come under his observation. The radiographic appearances showed very great similarity to those seen in tuberculosis.

In the discussion which followed, Potter stated that the X-ray appearances were very similar to those found in blastomycosis.

Bowman considers the name of the disease to be a misnomer; it is due to a mould-like growth and not to protozoa, and it is not the same organism as that found in rabbits. R. W. A. S.

Mougeot, A. et **Pacaud.** L'aortite thoracique descendante; son diagnostic radioscopique. [**The radioscopic diagnosis of aortitis in the thorax.**] *Paris méd.*, 1919, No. **45**, 374. (*Arch. d'électric. méd.*, 1919, **27**, 340.)

According to the authors, in contradistinction to ascending aortitis and abdominal aortitis, descending thoracic aortitis is inaccessible to clinical means of examination and can only be accurately diagnosed by radioscopic examination. The left side of the descending aorta, invisible under physiological conditions, is clearly distinguishable when pathological. When the first part of the descending thoracic aorta is dilated, there is an abnormal arciform shadow separated from the aortic arch and ending at some more or less low spot of the cardiac shadow. The descending aorta should be examined in the left lateral position, and very obliquely in the left anterior oblique position. Slightly visible when they are normal, the horizontal part of the arch and the first part of the descending aorta, when they have become opaque or dilated, form a shadow which is at first horizontal and then bends towards the vertebral column and becomes detached from the shadow of the scapular masses. The lower part of the descending thoracic aorta should be examined very obliquely in the left posterior oblique position. Its pathological shadow appears to the left of the vertebral column narrowing the clear cardio-vertebral space the more because there is, at the same time, hypertrophy of the left ventricle. S. U. L.-B.

Leguen, F. et **Papin, E.** La cystoradiographie. [**Cystoradiography.**] *Presse méd.*, 1919, Dec., 733. (*J. de radiol. et d'électrol.*, 1920, **4**, 137.)

Cystoradiography consists of radiography of the bladder after injection into its cavity of substances which are opaque or transparent to X-rays. If a clear image be required, air or oxygen is injected, while, preferably, a double-current probe is used, enabling one to replace the previously injected liquid by a corresponding quantity of oxygen; if a dark image be desired, either a 10 per cent. bismuth suspension is injected, or, preferably, collargol 3 per cent. to 10 per cent., or iodide of silver, sulphate of barium, or a thorium salt. In malformations of the bladder, and particularly in the case of diverticula, cystoradiography brings micturition into evidence in two stages; a first negative is taken with the bladder full; a second, obtained after micturition, shows, in most cases, the diverticula not evacuated.

Tumours of the bladder. Radiography is indicated after the bladder has been filled with an opaque liquid, in cases where an intense cystitis or haemorrhage hinders a satisfactory cystoscopic examination. In cases of large or medium-sized tumours it enables one to specify the situation and size before intervention. In hypertrophy of the prostate, cystoradiography is of no interest as it is generally useless for diagnosis.

In cases of insufficiency of the ureteric meatus one can see regurgitation of the opaque liquid into one or both of the ureters.

Radiography of vesical calculi may be helped by a previous injection into the bladder of oxygen (when the images of the calculi are dark and sharper) or of an opaque liquid (clear images of the calculi).

S. U. L.-B.

Japiot. Erreurs graves de la radioscopie du poignet. [**Serious mistakes in radioscopy of the wrist.**] *Progrès méd.*, 1919, **39**, 390. (*J. de radiol. et d'électrol.*, 1920, **4**, 136.)

The author reports two cases in which mistakes were made from the use of radioscopy alone in examination of serious traumatism of the wrist. In the first case there was fracture of the styloid process of the radius, fracture of the scaphoid, and comminuted fracture of the semilunar. These lesions were not brought into evidence until five weeks after the wound occurred, and then only because of the patient's insistence that he was in pain and had only very limited use of the wrist. Anterior radioscopy was entirely negative and the patient was told that no injury was visible on the screen. The second observation revealed a fracture of the radial epiphysis and of the styloid process of the ulna, with dislocation forward of the semilunar; but meanwhile, ankylosis of the wrist, compression of the median, and decalcification of the bones of the hand had supervened. The former radioscopy had only revealed a simple fracture of the styloid process of the radius. Therefore, stress should be laid on the point that radiography must be systematically employed in cases of traumatism of articular, and especially of polyarticular, regions. Radioscopy only produces illusory guarantees and leaves to radiography all the responsibility of revealing posterior injuries. S. U, L.-B.

Fernet, P. et **Nahan.** Un cas de concrétions calcaires sous-cutanées. [**A case of subcutaneous concretions.**] *Bull. Soc. franç. de dermat. et syph.*, 1919, **7**, 266. (*J. de radiol. et d'électrol.*, 1920, **4**, 138.)

The authors present the case of a patient of 16 years in whom, at the age of 15, subcutaneous calcareous concretions appeared at the ends of the fingers, then on the feet and at the knee. Development took place fairly rapidly. The tumours, rounded and uneven, raised the integument, which in certain places was extremely thin; where it had ulcerated, the opening allowed a whitish substance resembling diluted chalk to exude. Radiography revealed clear images of concretions larger than was expected from the clinical examination. The first impression was that the concretions followed the path of the vessels; the histological examination showed, round the calcareous nodules, a very marked reaction of the connective tissue cells. In this connective tissue reaction it was possible to distinguish capillaries undergoing endothelial proliferation and containing small masses of calcareous material. The whole condition seemed to be vascular in origin. Dermatologists term this affection 'subcutaneous calcareous granuloma'.

[The condition appears to have some marked resemblances to the 'chalk stones' of gout.—Ed.] S. U. L.-B.

Radio-technique

ZWALUWENBURG, J. G. VAN. A plea for the use of the fluoroscope in the examination of the heart and great vessels. *Am. J. Roentgenol.*, 1920, **7**, **1.**

This observer considers that it is not sufficient merely to determine the actual size of the heart. An attempt should be made to determine the relative size of the various chambers of the heart, and this, he thinks, is virtually impossible by radiographic methods as opposed to fluoroscopic. By the latter it is possible by direct observation of the cardiac movements to gain some idea of the vigour of the heart-muscle itself and of its relation to the other structures of the thorax, not only in a static but in a dynamic sense.

He compares the skilful internist and the radiologist. The former may discover two murmurs indicating two distinct lesions, as a murmur is qualitative and not quantitative evidence, while the radiologist finds but one. The latter, who has to judge by the consecutive changes in the size and volume of the heart or of its various chambers, finds evidences which are in direct ratio to the volume of the regurgitation, i.e. these evidences are quantitative rather than qualitative. In the presence of a major and a minor lesion, it therefore follows that he sees the evidence only of the major and overlooks the minor one.

The author considers that the orthodiagram is really a caricature rather than a faithful likeness of the cardiac outline. But just as a caricature is intended to bring out the individuality of the person's features, so the orthodiagram makes the distinctive features of its shape more conspicuous and the conclusion more obvious.

From a plate it is difficult to distinguish the point of division on the left border of the heart between the left auricle and the left ventricle. Its determination rests on the recognition of a point at which the ventricular motion differs from that of the auricular. At this point there is a sort of 'walking-beam action' with the formation of a 'node of no motion' which is not entirely stationary but moves up and down along the left border.

The author reminds us that the so-called oblique diameter extending from the auriculo-diaphragmatic angle to the left auriculo-ventricular junction roughly corresponds to the dividing line between the auricles and the ventricles. The area above and to the right is a rough index of the auricular area, and that below and to the left the ventricular area. He has attempted to reduce this to a numerical basis by using the ratio of the two segments of the long diameter as intersected by this line (*a.-v.* ratio). He admits that this ratio has many defects. The position of the auriculo-diaphragmatic extremity of the oblique diameter, for example, is not fixed, and depends much upon the level of the diaphragm.

In the estimation of the area of the heart, he continues the upper border of the left ventricle to join the auriculo-caval junction in a smooth curve and then similarly to close the lower opening of the cardiac shadow. The figure is approximately an ellipsoid and its area may be calculated without great error by applying the formula for the ellipse.

The author has expressed the size of the heart by the ratio of this area divided by the 'norm' for individuals of the same weight. This 'norm' was established on approximately 75 persons with apparently sound hearts. When these were plotted in a curve it was discovered that they closely approximated that represented by the following formula:

$$\text{area (sq. cm.)} = 3\sqrt[3]{wgt.^2}\,\text{(lb.)}.$$

This simply means that normally the weight of the heart varies directly with the weight of the body, and that the comparable areas on similar volumes vary as the cube root of the squares of these volumes.

The beginner is usually struck by the relatively small excursion of the apex. This follows from the usual conception that during systole the apex, by the shortening of the long diameter of the heart, approaches the base of the ventricle near the midline. As a matter of fact, the greater part of the shortening is accomplished by the descent of the base towards the apex.

If the heart is not well supported by the diaphragm, but is freely suspended from its attachment in the mediastinum to the deep fascias of the neck, the lower border is now free to move, and, in fact, the entire outline of the heart partakes in the movement as a response to the recoil from the effort of expulsion of the blood-stream into the aorta. The author thinks that this is the explanation of many of the throbbings and palpitations in this type of visceroptosis and neurasthenia. R. W. A. S.

Bergonié, J. Plates-formes isolantes de protection pour laboratoires de radiographie et radioscopie. [**Protective insulating platforms for radiographic and radioscopic laboratories.**] *Arch. d'électric. méd.*, 1920, **28**, 50.

In laboratories with cemented or tiled floors the author believes that one of the most important protective devices is that which insulates the operator from earth, and he describes a small movable platform, such as used in his laboratory at Bordeaux University. It is a rectangular framework 1 metre long and 50 cm. broad, built of deal of cross-section 4 × 4 cm., the sides being either dovetailed together or pegged with wood. Cross-pieces, 4 cm. broad, parallel to the shorter sides fit into a rabbet 2 cm. wide and 1 cm. deep, and are spaced 2 cm. apart. The framework is washed with boiling paraffin and mounted on four solid glass cones placed at the corners. The glass cones are set in conical holes drilled into small oak boards, and, for a rigid support, it suffices to screw the oak boards to the framework. Such platforms weigh 8·5 kilo. and may easily be placed where required. L. H. C.

Gunther, M. L. Précautions à prendre dans les installations radiologiques intensives. [**Precautions to observe in powerful radiological installations.**] *J. de radiol. et d'électrol.*, 1920, **4**, 544.

In using a powerful installation the strictest precautions must be observed. See that the metallic parts of the various pieces of apparatus used are earthed, preferably at two points, by connecting them to a central heating apparatus or water-pipe by means of flexible leads. It is better to use heavily insulated wires, but to treat them as if they were bare. Test any trolleys and, so that a break in the trolley wire does not endanger patient or doctor, stretch earthed metal wires at intervals across the room transversely, 20 cm. below the trolley wire. Choose such a main fuse as will allow little more than the maximum current required. When the X-ray bulb is close to the patient cover him completely with an earth-connected metal gauge, particularly when a Coolidge installation is used, thus obviating accident due to an involuntary movement of the patient. The fact that neither the filament of the bulb nor the pilot lamp glows is not conclusive indication of absence of current. L. H. C.

Radio-biology

Prime, Fredk. Lymphocytes and cancer immunity. *J. Cancer Research*, 1920, **5**, 105.

The author's experiments are concerned with the action of X-rays upon the rat's resistance to tumour growth.

Broadly speaking, the trend of the investigation has been to select a number of rats which were known to be immune to inoculation of tumour, submit them to doses of X-rays and re-inoculate them in order to see whether the immunity of the animal has been interfered with. Three strains of tumour were used in this investigation, namely, a Flexner-Jobling rat carcinoma, a sarcoma, R 10 Crocker Fund, and Jensen's rat sarcoma. With the doses of X-rays employed there was very little evidence that the immune process in the animals was interfered with, though a considerable decrease in the number of circulating lymphocytes was observed; in fact steps were taken by the author to keep the numbers of lymphocytes at a low level during such times as the test of tumour growth was current in the animal. These negative findings by the author are considered by him to discount the suggestions which have been made by various other experimenters that the lymphocyte is an active agent in the process by which the immunity is established and maintained in the animal body. It is equally permissible, however, to observe that what the author's experiments show is that, once established, the immune condition in the animal is something which it is exceedingly difficult to break down by an agent such as the X-rays, and it is of course nothing less than fortunate that stability should be one of the features of the process of immunity. The author seems indeed to be at some pains to discount lymphocytic activity as playing any real part in the immune process, yet most of his observations have been anticipated by work on similar lines to his own.

It has, for instance, been shown that although an enormous reduction in the circulating lymphocytes may occur, yet the animal retains its immunity, and it is only when the radiation is pushed to rather extreme limits that any breaking down of the immunity is put into evidence. Here, in fact, his findings run parallel to the observations mentioned, for we read, 'In all these experiments, it was found, just as was reported by Mottram and Russ, that occasionally a small tumour in the radiated animals would persist longer than one in the controls...' Here, then, is the key of the situation; the lymphocyte is an extremely sensitive type of cell to X-rays, a dose sufficient to rid the circulation largely of these cells is not sufficient to break down the established immune condition in the animal, but if the degree of radiation is pushed to greater limits, evidence of it is found.

From the two facts, first, that an immune rat may have very few circulating lymphocytes, and, secondly, that a rat may have its numbers of lymphocytes increased tenfold without the animal exhibiting any increased resistance to the growth of inoculated cancer cells, it is quite evident that whatever part these lymphocytes may play in the immune process it is not a part solely conditioned by their numbers in the circulation; this, however, by no means precludes their functioning in some essential manner in what is in all probability a highly complicated process. S. R.

Electrology

Gunsett et **Zimmermann.** Les cas de mort survenus après applications de courants sinusoïdal (dans l'armée allemande). [**Cases of death supervening applications of sinusoidal currents (in the German army).**] *Bull. Soc. franç. d'électrothérap. et de radiol.*, 1919, July–Oct., 48. (*J. de radiol. et d'électrol.*, 1920, **4**, 47.)

During the war several German authors related cases of death produced by application of the 'faradic sinusoïdal' current, of pantostats or of multostats. It was Kauffmann who, for the treatment of hysterical phenomena, extolled a sort of torpedoing with this current. Now, if faradization, formerly used, strongly excites the sensory nerves, while the mean intensity of the current, because of the shortness of the discharge, remains weak, with the sinusoïdal current, which gives an extended wave, sensation is much weaker and the mean intensity becomes more considerable: so much so that, as Boruttau indicated in 1917, the internal organs are fatally involved. The heart is particularly sensitive to these currents, which determine auricular fibrillation. The following facts, ascribable to Kauffmann's method, were published by Hering in 1917 in *München. med. Wchnschr.*, and it is clear that cases were actually more numerous.

I. Plot 8. Electrodes: breast—arm, sudden death from stoppage of the pulse. *Post mortem*: fatty degeneration of the heart of middle intensity, minute gumma in the left side of the heart.

II. Plots 9 and 10. Electrodes: xyphoid process—thigh; sudden death from stoppage of the pulse. *Post mortem*: hypertrophy of the thymus.

III. Plots 9 and 12. Electrodes: breast—hand; sudden death. *Post mortem*: thymus slightly enlarged.

IV. Plot maximum. Electrodes: nape of neck—breast; sudden death from stoppage of the pulse and of respiration. *Post mortem*: large thymus.

V. Plots 8 and 9. Electrodes: left breast—right arm: progressive slackening of the pulse, then stoppage of the heart and respiration. *Post mortem*: rather large goitre, thymus very little enlarged.

VI. Strong current; sudden death: hypertrophy of the thymus.

VII. Medium current; sudden death: hypertrophy of the thymus.

VIII. Plots 7 and 8. Electrodes applied in various places: back, chest, abdomen, &c.; sudden death: hypertrophy of the thymus.

The voltage in all these cases was 50 to 70, the periodicity 60 to 65. As one can see, all the cases were subjects of changes predisposing sudden death; other cases can be found in German literature where death supervened on applications of sinusoïdal current without Kauffmann's extreme technique having been employed.

Lewandowsky, for example, saw a young man fall dead at the beginning of a very weak application; the two electrodes were placed one on each side of the vertebral column (hypertrophy of the thymus existed in this case also); he came to the conclusion that the sinusoïdal current should be banished from the medical arsenal.

Boruttau recalls the fact that the alternating current can kill by stopping the heart with 100 milliamperes: now panto-stats require 60 to 70 volts and 100 ma. are obtained when 30 volts have been reached if things be arranged so that the resistance of the body is 300 ohms. Further, it is certain that a diseased or weak heart will begin to show fibrillation before the current reaches 100 ma. The conclusion is that the sinusoïdal current cannot replace faradism. S. U. L.-B.

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ABSTRACTS & REVIEWS

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REVIEWS

A CRITICAL REVIEW OF THE CANCER PROBLEM

General

Apart from the fact that cancer is probably one of the most difficult problems set to the biologist, and therefore that rapid advance is not to be anticipated, it is only since the beginning of the century that modern research methods have been systematically applied to its solution. Although the Cancer Charity at the Middlesex Hospital—the first of its kind—was founded in 1791 for 'the relief of persons afflicted with cancer, and the investigation of a complaint which, though extremely common, is, both with regard to its natural history and cure, but imperfectly known', little beyond the collection and collation of records was undertaken until 1899, when the Cancer Research Laboratories were established.

Since 1899, institutions and foundations for Cancer Research have been established in England, America, France, Germany, Japan, and other countries. Of these, the most important are the Imperial Cancer Research Fund and the Foundation at the Middlesex Hospital in England, the Harvard University, the Columbia University, and the Gratwick Foundations in the United States, the 'Association française pour l'étude du cancer' in France, the 'Komite für Krebsforschung' in Germany, and the Society for Cancer Research in Japan. At the time of writing a large institute for treatment and research is approaching inauguration in Buenos Ayres. Each of these institutions has laboratories attached, and periodically publishes official scientific reports.

In addition, since the commencement of the century, a few hospitals (e.g. das Samaritarhaus in Heidelberg) have been founded for the treatment of cancer patients and prosecution of research, and numerous institutes have been opened all over the world for the treatment of patients with cancer and other diseases, by means of radium.

And lastly, the formation of a radiological department controlled by a specialist in his subject at every hospital of any importance has led to sporadic treatment of cancer with radium and (owing to the scarcity of radium and the close relationship of hard X-rays to the gamma-rays of radium) to an extensive treatment of cancer by means of X-rays.

It follows that the literature of cancer research during the past twenty years has grown considerably, both on its laboratory and on its clinical sides. Much of the laboratory work suffers from the fact that it is too academic: much of the clinical work suffers from too little scientific accuracy. Of these faults the latter is the worse, since the conclusions drawn by the authors are often quite unreliable; academic investigations carried out in a scientific manner may present conclusions of which the application is not apparent at the moment, but, at least, they are definite contributions to knowledge, and to that extent are valuable.

In order to consider the present position of cancer research the subjects of the cause and the cure cannot be separated. In the case of many investigations it is difficult to decide whether they are more designed to elucidate the natural history of the various conditions grouped together under the one name of cancer, or designed towards the actual treatment of patients suffering from cancer. Though distinct they are ultimately destined to find their application in the patient, and, in this respect, are as closely related as pathology and pharmacology.

No doubt, when it was considered that cancer was a single disease it was thought that discovery of a single cure was possible. And medical literature is full of examples in which some substance or method of treatment was vaunted as a specific. The fact that each of these, in turn, was found to be valueless when examined clinically, and that the only method offering the slighest hope was surgical operation, led to extensive examination of the primary concept of cancer.

First came the differentiation into the two great groups of carcinoma and sarcoma, followed later by recognition of the endotheliomata. Each of these two groups was further subdivided according to the nature or shape of the cell involved. Continued study led to recognition of a number of special types of growth which could not be included easily in the old groups, so that the hypernephroma, the melanoma, the myeloma, &c., were split off. This practice is still in operation, for, in recent years, the seminoma, the paraganglioma, and the parasympathoma have been described by French authors. Thus the range of the subject to be investigated has extended in ever widening circles, even if considered merely from the anatomical (or embryological) and descriptive side.

In the meantime, progress in other branches of medical science suggested new series of investigations into the still unsolved problem. Bacteriology and microparasitology were examined as possibly holding the clue, since cancer has manifest similarities and relationships with inflammatory conditions dependent upon bacterial and parasitic causes. No important successes followed these lines of investigation. They raised the suspicion that the sarcomata might be of different aetiology from the carcinomata, and suggested that some so-called sarcomatous conditions were, in reality, infective granulomata, and therefore should be excluded from the cancer group altogether. Nevertheless, this line of research cannot be ruled out of court entirely, since a new group of diseases occasioned by 'filter-passers' has been recognized of recent years, and in certain of these (e. g. poliomyelitis) the infective character, though present, is not striking, except under experimental conditions. Similarly, on the microparasitic side, Leishmania and Rickettsia have opened up new vistas. Though bacterial and parasitological investigation of cancer has everywhere fallen into abeyance, it is possible that it will have to be revived under modern conditions.

Similarly, physiological and pathological chemistry have advanced into the foreground. Given that certain cells multiply to form a tumour the chemical conditions in the parent body immediately antecedent to the occurrence of that tumour and those subsequent to its development probably differ from the normal. If the antecedent changes could be determined, elucidation of the 'cause of cancer' would be greatly facilitated; if the subsequent changes were known, 'cure of cancer' would be nearer and treatment more satisfactory. In this division of the subject, as in all others, we are dependent upon a knowledge of the normal. But physiological chemistry is in its infancy, so that it may fairly be said that each investigator on the chemical side of the cancer problem, before inquiring into variations from the normal standard, will have to determine for himself the limits of the normal. Not infrequently he will have to devise methods for attacking this initial difficulty.

And, to bring the matter up to date, discovery of the X-rays, radium, and other radio-active substances has introduced entirely new methods of envisaging and attacking the cancer problem. At first, X-rays were employed empirically, as a potent agent which might possibly be of use in treatment of cancer. But soon—through the fact that numerous workers with X-rays began to suffer from cancer of the hands—it became recognized that X-rays are closely associated with the onset of cancer in certain cases. Numerous attempts were made to produce cancer experimentally in lower animals by their means on the view that, when the disease can be produced at will, experiments for its prevention and cure can be carried out with greater hope of success. Simultaneously, the researches of physicists led to the recognition of the fact that the rays emitted by the X-ray bulb and the gamma rays of radium consist of waves forming definite portions of a spectrum that extends far beyond the violet end. And, partly from the physical, partly from the chemical, partly from the biological, and partly from the medical side, it was shown that difference of wave-length was associated with difference of effect. Hence, in the case of animal cells, has arisen the almost universal belief that the rays exert a selective action. This leads to the further conclusion that, by irradiation with waves of a specified length, cells of a specified kind can be affected to the greater or less exclusion of all others. Dosage of rays and the state of the cell in respect of division are factors of great importance in this connexion, and must necessarily affect the result to a considerable degree.

It follows from the above that the cancer problem is being attacked from the anatomical (including embryological and surgical), the chemical and the radiological sides in the laboratory and in the wards. It is essentially a problem of division of the animal cell, and, as such, is concerned with the fundamental laws of growth and nutrition, which must be investigated in the living as well as in the dead. The scope of cancer research is therefore equally wide, and in prosecuting that research every advance in physiological chemistry or in radiology is potentially a help. If the region to be explored is now seen to be greater than was thought at one time, the means of exploring it have also increased. For the investigators, however, this dual expansion makes the research even more difficult. From the point of view of literature alone the number of periodicals and published papers which the worker finds it necessary to consult is so great and is increasing so rapidly that consideration and co-ordination of cancer literature becomes an important, though tedious and laborious, part of cancer research.

Work of the last Twenty Years

In one form or another the statement is often made that we are no nearer to a solution of the cancer problem than we were twenty years ago. How loose and untrue is this statement can be seen from the following list of facts with direct bearing upon the cancer problem that have been accumulated during the last twenty years. I have divided them into General, Histological, Chemical, and Radiological, though a given fact might often be placed under several headings. It is not claimed that the list is complete or beyond controversy, and important facts known previous to the period under consideration (e. g. the association of cancer with certain specific varieties of irritant, such as tar, paraffin, soot, use of the kangri, dhobie-string) are not included.

General.

(1) In England and Wales one woman in eight and one man in eleven above the age of 35 years dies of cancer.

(2) Cancer occurs in all races of mankind.

(3) Cancer occurs in many species of animals.

(4) Cancer occurs independently of racial peculiarities of diet.

(5) The site distribution of cancer differs in different parts of the world.

(6) The age distribution of carcinoma and of sarcoma are different.

(7) Cancer in certain rodents is transmissible from one animal to another of the same species by inoculation of living cancer cells.

(8) Disappearance of isolated secondary nodules and, in a few instances, of the entire disease has been known to occur in man apart from treatment.

(9) Acquired immunity to transplanted cancer in the mouse and rat can be produced by means of *living* cancer cells.

(10) In certain plants, tumours homologous with some varieties of tumours met with in man have been produced experimentally by means of bacterial inoculation.

Histological.

(11) Altmann's granules are absent from malignant growths and their metastases.

(12) As a result of perilymphatic fibrosis, foci of cancer cells may undergo pressure atrophy and disappear.

(13) Certain strains of tumour in mice, which were originally of carcinomatous type, have been found, after repeated propagation in mice, to change their type into that of sarcoma.

(14) In the case of certain malignant tumours of rat and mouse the production of acquired immunity is directly associated with a great increase of plasma cells and lymphocytes in the spleen and probably other tissues.

Chemical.

(15) The blood and tissues of carcinomatous persons contain more potassium than normal.

(16) Chemical changes, mainly of a disruptive kind, have been found to be produced by the action of X-rays and radium.

Radiological.

(17) X-rays cause cancer, directly or indirectly, in man and (experimentally) in lower animals.

(18) By experimental introduction of radium, epithelial changes resembling those of cancer can be produced in the skin of the rat and gall-bladder of the rabbit.

(Nos. 17 and 18 must be correlated with the experiments of Fibiger, who produced cancer of stomach and tongue in rats by feeding them with a certain variety of infected cockroach, and with those of Yamagiwa and Ichikawa, who produced cancer in the ears of rabbits by repeated painting with tar.)

(19) Human cancerous tissues contain more radium than normal.

(20) Gall-stones associated with cancer of the gall-bladder in man contain more radium than gall-stones unassociated with cancer or associated with cancer in other parts of the body than the gall-bladder.

(21) The division of animal cells can be stimulated by exposing them to the action of suitable quantities of radium rays.

(22) Exposure to greater quantities of radium rays than those leading to stimulation brings about degeneration and finally death of the cells.

(23) Cells are most vulnerable to the rays of radium when in a state of active nuclear division.

(24) The dose of X-rays or radium rays lethal to malignant cells of rat and mouse has been determined within narrow limits. There is reason to believe that the lethal dose for the cell of human spheroidal cell carcinoma is approximately the same.

(25) Other factors being constant, different varieties of cells behave differently to radiations of a given wave-length.

(26) Normal columnar and squamous epithelia of rat react in different degrees to the same total dose of gamma radiation from radium. If Q or $q =$ large or small quantity of radium, T or $t =$ long or short time of exposure, and $Qt = qT$, Qt produces far more change in columnar epithelium, qT produces far more change in squamous epithelium.

(27) In the case of rat tissues exposed to the gamma rays of radium and covered respectively with columnar and with squamous epithelium the complex 'interference with multiplication of epithelial cells combined with avoidance of damage to supporting tissues' is greater when the radium is heavily screened than when it is lightly screened.

(28) By means of the Coolidge tube an exactly measured dose of X-rays of known hardness can be administered. Similarly, the dose of radium rays administered can be determined with accuracy.

(29) Treatment by radiations has been followed by temporary disappearance of a malignant growth and restoration to health in many cases, and in a certain number of cases health and absence of local or systemic recurrence have persisted for three or more years.

(30) The amenability of different varieties of tumour to radiological treatment is not the same under present methods of treatment.

(31) The gross dangers of X-rays and radium treatment are largely known and can be guarded against.

(32) New growths of internal parts may frequently be diagnosed by the aid of radiography, with or without the administration of contrast meals, which formerly were only a matter of suspicion during life.

If a broad view be taken of these facts, it appears that work has proceeded in three main directions:

I. Attempts to produce cancer in lower animals.

II. Experiments to interpret the phenomena of natural and acquired susceptibility and immunity to cancer.

III. Experiments to investigate the action of radium and X-rays conducted upon the widest lines.

The results obtained in these three spheres of work have been very different and merit some consideration.

I. Attempts to produce cancer in lower animals really depend upon a belief that spontaneous and transplanted cancer are not identical. This view is at the bottom of the deep-rooted objection on the part of the clinician to attach importance to experiments on mouse and rat cancer. Not a few pathologists are ready to agree in respect of transplanted tumours, but the life-history of an animal in which a spontaneous malignant growth has occurred—its local recurrence after removal, its infiltration of neighbouring tissues, its liability to produce metastases, its resistance to remedial agents of all kinds, its ulceration, and the fatal result—are so similar to what obtains in man that the two spontaneous forms may well be comparable for experimental purposes. If this be so, then the impossibility of subjecting human patients to satisfactory experimental conditions enforces the necessity of 'producing' cancer in a laboratory animal, so that the investigation may advance. It is not certain that an animal with 'produced' cancer will behave in the same way as one with spontaneous cancer, but there is some evidence from the work of Clunet and the recent work of Fibiger that this may be the case.

One of the most striking points about all experiments with the object of producing cancer is the comparative ease with which a local proliferation of tissue can be induced and the readiness with which it reverts when the experimental agent of stimulation is removed. The investigator has the sense of an intensely powerful resisting influence on the part of the animal against extension of any proliferative process artificially produced. Hence this type of experiments is now being combined with procedures calculated to break down the natural resistance. In hitherto unpublished experiments conducted during the past two years, I have endeavoured to combine local stimulation of cells by means of small quantities of radium with general lowering of resistance by means of feeding with potassium or administration of X-rays. The results are not as good as was hoped would be the case, but they tend in the right direction. Incidentally, they suggest that *potential* cancer only becomes converted into *actual* cancer when some underlying natural resistance on the part of the individual is wanting. Clearly the factors constituting that resistance may be present at one time or age or under one set of conditions and absent at another even in the same individual. And clearly for their elucidation a great extension of our knowledge in biochemistry is necessary. This is the old controversy as to whether cancer is a local or constitutional disease presented in a new and less exclusive form.

Some experiences suggest that this view is not unreasonable. Thus, in treatment of rodent cancer, cases are met with in which there is an apparently arbitrary contrast in behaviour of the growth under X-rays and radium. Similarly, the greater resistance of a growth to the later irradiations of a series may depend upon modification of the host as well as upon modification of the tumour cells. And one of the most satisfactory results in cases of cancer of the breast that were obtained when experimenting with 5 grm. of radium bromide (see below) was that of a woman who had previously suffered from a cancer of the opposite breast which had entirely disappeared under X-ray treatment. In this case it seemed as if the underlying conditions in the patient were such that she was able to utilize X-rays and radium rays for the removal of a malignant growth in a way and to a degree that are unusual. Cases of spontaneous recovery from malignant disease argue in the same direction, and it may be that they would not be so seldom seen if we were cognizant of the earliest beginning of cancer.

So far as concerns the initial proliferation of cells in cancer it does not seem probable that this will be occasioned by a single agent or even by a single group of agents. On the other hand, it is probable that increasing knowledge will find a common factor in many different so-called causative agents. And yet no simplification is introduced by saying, for example, that clay pipes, tar, X-rays, *Spiroptera neoplastica* of cockroaches act by way of the 'chronic irritation' they exert. Nor will it help much if—following the modern tendency—the explanation be referred to electronic action.

II. Investigation of the phenomena of natural and acquired susceptibility and immunity in cancer has been the basal idea in the great majority of experiments upon transplanted mouse and rat cancer throughout the world. It has led to the accumulation of much knowledge upon the natural life-history of malignant tumours in rats and mice, and notably to recognition of the fact that the tumour cells are not mere passive agents but also have a share, as well as the host, in determining whether a tumour shall be of the progressive or oscillatory or the retrogressive type. Occasionally two grafts of the same rat tumour inoculated into the two sides of one rat may grow equally for a time and then diverge in behaviour, the one continuing to progress while the other retrogresses. In man, a similar difference of behaviour may characterize subcutaneous nodules in cancer of the breast. That the real explanation in this case lies in the tumour cell is seen from the fact that one can, by suitable irradiation of tumour cells, convert a progressive type of Jensen's rat sarcoma into an oscillatory or a retrogressive type.

A further result of this line of research has been the recognition of a marked difference between spontaneous and transplanted animals in respect of immunity. Largely by the work of the Imperial Cancer Research Fund, this has been shown in three directions:

(1) The natural susceptibility to autologous grafting in an animal with a spontaneous tumour as compared with the great natural immunity residing in other animals of the same species.

(2) The co-existence of this natural susceptibility to autologous grafting with a natural immunity to grafts from another source, and

(3) The possible co-existence of this natural susceptibility to autologous grafting with an acquired immunity to readily transplantable grafts of a heterologous tumour.

From this it is seen that the specificity of tumour cells is remarkable. Histological similarity does not imply biological identity. Hence it would appear that though *A* and *B* suffer from carcinomata of the tongue which are indistinguishable under the microscope, relief for *A* will ultimately be obtained by way of using *A*'s tumour cells; relief for *B* will ultimately result from a similar but not necessarily identical use of *B*'s tumour cells.

How far the difference between natural susceptibility to autologous grafting and natural immunity to heterologous grafting is one of kind or of degree, it is impossible to say at the present time. Some investigators believe that if a means be found to induce an extremely high degree of immunity to an easily transplantable tumour it will prove to be a means of inducing immunity in an animal with a spontaneous tumour to autologous grafting. That is to say, such a method should be applicable to spontaneous tumours in general and therefore suitable to therapeutics in man. Other investigators incline to the belief that the difference is one of kind and not merely of degree. They hold that no amount of work with transplanted tumours will directly lead to the discovery of a means of treating spontaneous tumours successfully. Probably this view is justified in respect of immunity produced by other than radiological methods. But it has been shown at the Middlesex Hospital that suitable irradiation of grafts of Jensen's rat sarcoma outside the body, or suitable irradiation of the animal subjected to transplantation, may eventuate in the production of an immunity. And at the Rockefeller Institute it has been found that, whereas autologous grafting is successful in approximately 100 per cent. of cases, when the animal has not received X-rays, it is unsuccessful in approximately 50 per cent. of cases where the animal has received a suitable dose of X-rays between removal of the tumour and its re-inoculation. From these two sets of experiments it is argued that there is no essential difference between the spontaneous and the transplanted animal, but that by means of irradiation it is possible to produce an immunity to malignant cells in both. Much more research is necessary upon the point, but recent clinical experience of X-rays and radium in the treatment of malignant disease lends support to the last-mentioned view.

III. Experiments to investigate the action of radium and X-rays were, in the first instance, of a physical or physico-chemical character, and the living cell (whether animal or vegetable) was rather an incidental than a fundamental object of consideration. But it soon was recognized that the rays are capable of producing great changes, that all cells do not react in the same way to a single dose of irradiation, and that research was necessary before the relations between animal cells and radiations were sufficiently understood for radiological treatment to be placed upon a sound basis.

One of the earliest and most important points determined was that exposure to rays may be followed by stimulation of the cell under one set of conditions and degeneration under another. This observation lies at the root of all radiotherapy of malignant growths in three ways:

(1) The malignant cell may be destroyed locally and stimulated to increased growth at a distance, owing to the fact that the intensity of irradiation falls off, roughly, according to the law of inverse squares.

(2) The connective and other reparative tissues may be destroyed or stimulated locally.

(3) The natural resisting powers of the individual may be enhanced or reduced generally.

Obviously an ultimate beneficial effect of the radiotherapy must depend upon a nice balance of these various factors. The question is one of great importance. Many clinicians have expressed the opinion that neoplasms may take on enhanced growth after an irradiation, or that the patient's health may deteriorate more rapidly than would be expected. And recently three cases of acute cancer during deep X-ray therapy for uterine fibroids were reported, at the Société de Chirurgie in Paris. In the *Journal de Radiologie* the question is being discussed whether the irradiation occasioned the carcinomata or, at all events, stimulated them into activity.

At the present time, investigations are being carried out at the Middlesex Hospital with 5 grm. of radium bromide lent for experimental purposes by the Medical Research Council. The results are not yet ready for publication, but it may be stated that the investigation has been partly on cancer patients and partly on animals. So far as patients are concerned, striking immediate results have been seen in cases of lympho-sarcoma and some other conditions, but it is still too early to express confident opinions. One indication, however, of the distance that radiotherapy of malignant disease has travelled in the past twenty years lies in the fact that cases of rodent cancer have been excluded from the investigation. It has been taken as proved that this form of malignant disease is amenable to irradiation.

Three observations in patients are of interest in connexion with the animal experiments. They are (1) that the irradiation sometimes leads to nausea and vomiting, especially if the lower thorax or upper abdomen be the region under treatment; (2) that the mucoid change in cells normally forming mucus or liable to undergo mucoid degeneration is pronounced; and (3) that the irradiation is succeeded by a fall in the number of lymphocytes in the circulating blood and a shrinkage in any great mass of lymphocytes (e.g. lymphosarcoma, lymphadenoma, lymphadenitis). The experiments on frogs, rats, rabbits, and cats, agree in showing (1) a marked degeneration of the gastric and intestinal mucosa—perhaps with haemorrhage; (2) an intense and widespread mucoid degeneration; and (3) a recognizable destruction of lymphocytes associated with measurable diminution in size of the spleen. Hence the parallelism is remarkable. Incidentally it may be mentioned that experiments with this large quantity of radium show that two great factors in the disappearance of new growths under rays are mucoid degeneration of the cytoplasm of the neoplastic cell and disintegration of the nuclear chromatin. These appear to be independent phenomena, for cells may show either of them or both.

Simultaneously with this investigation on the effects of a large quantity of radium, experiments (also on behalf of the Medical Research Council) are being conducted at the Middlesex Hospital on the effects of small doses of X-rays. Two interim reports have been published, in which some of the results bear on cancer. It has been shown that in rats there is some relation—not necessarily causal—between lymphocytes on the one hand and immunity or susceptibility to transplanted Jensen's rat sarcoma on the other. Further, it has been shown that an immunity to transplantation in a naturally susceptible rat can be built up by repeated small doses of X-rays, and on the other hand that a natural immunity can be broken down by administration of a single large dose of X-rays. There is not entire agreement between English and American workers on these points, perhaps owing to differences in the tumour used for grafts, or differences in the mode and degree of irradiation, or it may be more than one essential type of cell is concealed beneath the general name 'lymphocyte'.

INHERITANCE IN CANCER

The problem of inheritance, like that of a possible increase in cancer, has not been solved. So many factors enter into the calculations that for every author who concludes in the positive sense there is one who concludes in the negative. Much careful work has been done on the subject of inheritance of cancer in mice by Miss Maud Slye of Chicago. The work has been in progress for many years and the author holds strongly that cancer is a disease to which there is a marked hereditary tendency. But apart from some doubt as to the divergences from normal growth which Miss Slye allows herself to consider as bearing directly upon the cancer problem, it is a fact that the inbreeding in her mice is extreme. The original stock was limited to three animals, and upon the descendants of these three the research was conducted. It is possible that a more or less academic problem has been answered, and it must be allowed that the genealogical trees in her communications substantiate her conclusions.

From a practical point of view, the chance of inheritance in cancer is deemed to be so slight by the actuaries and medical referees of some important life assurance companies that no increase in premium is demanded if one parent of a proposer has died of cancer. The subject was dealt with by Orr in a paper upon 'The Selection of Lives' in the *Transactions of the Faculty of Actuaries*, and he concludes that, though it is necessary to keep an open mind on the matter, 'it is always possible, and even probable, that further medical research may show that, if there be hereditary influence in the occurrence of cancer, that influence is small'. He recommended that 'a reasonable attitude, or compromise, is to regard the occurrence of one case of cancer (in proposer's own family) as not preventing acceptance on ordinary terms, and to regard the occurrence of two cases as calling for the imposition of an extra premium'. In this connexion the 'local' and 'constitutional' views of cancer will incline beliefs, but it is at least possible, even though cancer be regarded as an 'acquired characteristic', that the chemical constitution of the body upon which the cancer is implanted is directly influenced by the chemical constitution of its parents.

Diagnosis of Cancer

At one time it was thought that a distinct advance in diagnostic methods had been introduced by a modification of the Abderhalden reaction. But quite apart from the slow and laborious character of the test, it was found to be unreliable, probably owing to accidental contamination with bacteria and the occurrence of proteolytic changes in the albuminous fluid subjected to dialysis. From Drummond's work on the composition of normal and tumour proteins, such a close correspondence is shown, that useful results in the direction of serological diagnosis are hardly to be expected.

Examination of test meals and determination of the free-acid secretion are carried out occasionally when there is a suspicion of malignant disease in the stomach. Here the grave disadvantage lies in the procedure necessary for the test meal. Unless it be carried out scrupulously the examination is almost valueless. Under any circumstances it is unpleasant for the patient. Nevertheless there is reason to believe that in most cases of gastric carcinoma there is great diminution or a complete absence of free hydrochloric acid.

In the case of the gastro-intestinal tract all methods of diagnosis have yielded to radioscopic or radiographic examination after administration of a bismuth meal. The technique of this procedure has been elaborated by many workers, particularly in America and France. The best composition of the bismuth meal, the normal appearances of the various parts of the gastro-intestinal tract, and the length of time after administration of a bismuth meal before it appears at given points of the alimentary tract have been studied. Turning to the pathological side, the significance of increased rapidity or delay in passage of the bismuth meal has been determined and, in particular, the modifications of the picture due to obstruction or ulceration are known. Actual diagnosis between a malignant and a non-malignant lesion must, of course, depend upon other criteria, but the method has rendered possible a diagnosis which formerly was one of probability alone, unless it was substantiated on the operating or the post-mortem table.

Histological diagnosis of malignancy or non-malignancy in the case of material removed by operation has been, in my opinion, greatly facilitated by Beckton's work upon Altmann's granules. The matter is not beyond controversy, and it is certain that the conditions of fixation of the tissues are so stringent that one cannot argue from animal to human tissues without great care. But, if Beckton's method be employed scrupulously, there is reason to believe, *caeteris paribus*, that absence of the minute Altmann's granules in cells argues for their malignancy, the presence of granules argues for their non-malignancy. Use of such a criterion in the case of material which may be inflammatory or sarcomatous is indicated strongly.

TREATMENT OF CANCER

It is still customary to describe cancer cases as 'operable' or 'inoperable' in spite of the fact that the 'operable' of one surgeon may be the 'inoperable' of another, owing to extent of growth and difficulty of access, character of growth, &c. Nevertheless, radium and X-rays have introduced a profound modification of procedure in certain directions, and it may be that they are destined to influence treatment to an even greater extent in the future. There can be doubt that, whereas in the past the choice was between surgery and no interference, at the present time it is between surgery and radiological treatment. It is fully granted that radiotherapy may be beneficial when surgery is impossible, and the view is gaining ground that the best treatment lies in some combination of surgery and irradiation, even in frankly operable cases.

In a strictly surgical direction, recent advances have not been of a fundamental kind. Handley's operation for carcinoma of the breast, based upon his histological recognition of the radial spread of cancer, the same author's operation of lymphangioplasty to relieve oedema of the arm from axillary invasion, and Wertheim's panhysterectomy are types of operations for more extensive and complete removal, based on anatomical lines, or operations of a frankly palliative nature.

On the other hand, radiological treatment in the past has been carried out by surgeons who were completely unacquainted with the agents they were using, or by radiologists whose knowledge was only one degree less imperfect. It was not until the lethal dose for cancer cells had been determined with approximate accuracy by Russ, in conjunction with Wedd (Twort's mouse carcinoma), Chambers (Jensen's rat sarcoma), and Mottram (human spheroidal cell carcinoma of breast), that it was possible to recognize that some cases of new growth which had been subjected to radiation had never received a dose lethal for the peripheral cells. There is room for difference of opinion as to the degree to which the cells of a malignant growth must be altered by the irradiation according as it is believed that the action is solely a direct one upon the malignant cells or partially indirect by way of the body fluids. But there is no room for surprise at an unsatisfactory result of irradiation when it can be shown that the peripheral cells have received a dose which is so far short of being lethal that it may well have been stimulating.

Similarly the fact that two apparently identical growths behave differently under irradiation cannot be ascribed with certainty to the tumour or the host, until it is certain that the treatment has been identical in the two cases. The extensive literature pertaining to the radiological treatment of new growths is so generally devoid of data upon which a sound opinion can be given of the degree of irradiation to which the malignant cells have been exposed that it is almost valueless. Attention to this point is one of the desiderata for the immediate future. Fortunately the Coolidge tube has rendered such standardization of dose possible in the case of X-rays, and Russ has devised a method for interpreting X-rays in terms of gamma rays of radium or vice versa. In regard to radium, careful determination of distance is of peculiar importance. It is easy to believe that the effective radiation at a distance of 2 centimetres is one quarter of that at 1 centimetre, but though the ratio is equally true at 1 or 2 millimetres (if the radiation come from a point source) it is far more difficult to appreciate in the treatment of a case. In the latter instance the surgeon or radiologist may believe he is giving the same dose, but actually he may be giving a fraction or a multiple. In using a flat applicator, this difficulty does not come in to the same extent.

Reference has already been made to the specific vulnerability of cells to irradiation. Quite apart from the different penetrating power of alpha and beta rays of radium and other radio-active substances, of 'soft' and 'medium' X-rays, of 'hard' or 'filtered' X-rays, and of gamma rays of radium, and the different degrees to which the tissues may react when exposed to one or other or several of them, there is no doubt that cells themselves differ in the degree of their vulnerability. Within the blood-vessels of a rat the lymphocytes will disappear while the polynuclear cells remain unchanged; in the kidney of a cat exposed for 24 hours to the action of the gamma rays of 5 grm. of radium, the convoluted tubules show intense lipoid degeneration, but the conducting tubules and glomeruli show no trace; spermatocytes and spermatoblasts of the rat show more pronounced changes than spermatogonia under radium or X-rays; the hair of rats exposed to a dose of X-rays, short of that necessary to cause epilation, may simply suffer a complete loss of pigment; the liver of frogs or of rabbits undergoes a marked destruction of the hepatic cytoplasm under heavy irradiation with radium. And in the case of the rat, squamous and columnar epithelium have been shown to react differently to a single total bombardment with gamma rays of radium according as the quantity of radium and time of exposure are large or small. It is important to note that Pinch, in the last report from the Radium Institute, finds that squamous carcinoma reacts better to a relatively small dose of radium acting for a long time, columnar carcinoma better to a relatively large dose of radium acting for a short time. *A priori* it may be expected that the spheroidal cell carcinoma, the endotheliomata, and the various types of sarcoma will require special adjustments of quantity and time if they are to be treated by radium with success. Probably the same is true with regard to treatment with X-rays, but as yet it is uncertain how far radium and X-rays can replace one another, if at all.

In addition to the local treatment of growths by irradiation alone, it has been added to operation with a view of preventing recurrences. Under these conditions it has been termed a 'prophylactic irradiation' but has generally been given *after* the operation in the form of five or six weekly doses of X-rays over the field of operation.

The process of reasoning is clear. The surgeon makes as wide a removal of the growth as possible, but is aware that outlying foci of malignant cells may be left. He knows that X-rays may be useful in killing malignant cells, and the irradiation is given with this object. But recent work has indicated that the rays act on more than the malignant cells, that a lethal dose for them may act injuriously on the patient (who has already been subjected to a more or less severe operation), that metastatic cells may be more widely disseminated than was supposed, so that far outlying nodules may receive a stimulating dose. Hence a tendency has arisen, largely at the instance of Nogier, to administer X-rays *before* the operation and over the outlying portions of the growth. Similarly in the case of radium treatment there is a tendency to replace the old method of inserting a tube of radium into the centre of the growth by a method of surrounding the growth with several tubes of radium and subsequent removal of the mass surgically. Clearly, if one can only deal satisfactorily with the peripheral cells of a malignant growth, treatment of the central mass is relatively simple.

Under these conditions, however, danger from another side must be guarded against. If the skin be subjected to too severe an irradiation, whether from X-rays or gamma rays of radium, its vitality may be impaired to such an extent that defective healing or even sloughing of the flaps made at the subsequent operation may occur. And, similarly, such a degree of irradiation as is associated with a pronounced and long-standing lymphopenia in the patient is not likely to be entirely beneficial, though from a purely *growth* point of view it might be so.

It is impossible here to enter into details of radium treatment as applied to growths in various parts of the body, particularly when special appliances are necessary, as in treatment of uterine, laryngeal, or vesical new growths, or when diathermy, electro-coagulation, or fulguration is added to the radium treatment. But reference may be made to the insertion of minute glass tubes of radium emanation into growths as introduced by Joly and Stevenson of Dublin and extensively practised at the Memorial Hospital, New York. The quantities of emanation introduced are small, and as they fall to half value in 3·86 days, they are left *in situ* or allowed to ulcerate out. The method is alleged to be highly successful, and is worthy of trial and perhaps extension. The principle upon which it is founded lies partly in the use of beta radiation, partly upon the prolonged use of small doses. One great advantage of the method appears to be the strictly localized action of intense radiation. If slight irradiation of the body in general be desired, with the object of building up an immunity, it can be carried out by other means. On the other hand, use and preparation of emanation tubes on a large scale is not without dangers to the personnel engaged. Mottram and Clarke at the Radium Institute, London, have shown that marked changes can be detected in both white and red cells.

Another method which is in its infancy consists in the use of active deposit directly obtained from radium emanation. It is either collected upon needles, which are thrust into the tissue to be treated, or on the surface of lead foil, or it is deposited upon salt crystals, which are subsequently injected intravenously, intraperitoneally, or subcutaneously in the form of a radio-active saline solution. The method is not without its special dangers.

Conclusions as to the efficacy of treatment of malignant disease by modern methods are not easily made. The surgeon whose experience of radiology is confined to his own attempts in cases that he deems surgically inoperable, is likely to meet with far more disasters than successes. The radiologist who only treats patients sent to him as a last resort, cannot expect his still imperfect methods to work miracles. The pathologist who lives in the post-mortem room perforce takes a pessimistic view of treatment in cancer, whether surgical or radiological. And, under any circumstances, it is impossible to say that a patient, who is alive a certain number of years after undergoing a given line of treatment, would not have been alive in the absence of that treatment.

Hence the statistical results are not fully satisfying. There is no doubt that the records of surgical methods (e. g. in carcinoma of the breast) have shown a continuous improvement, and there is little doubt that the records of Radium Institutes are usually tinged with optimism. Nevertheless, when all allowances have been made, the increasing use of radium and X-rays in the treatment of malignant disease, the general agreement as to a special amenability on the part of rodent cancer to irradiation, the remarkable—if temporary—results that are obtained in lymphosarcoma, lymphadenoma, and some other conditions, and the steady accumulation of histological data showing the profound influence of rays upon cells, form a mass of evidence which cannot be gainsaid.

Whether, in future, chemotherapy will come to the front it is impossible to say. Pinch has found that, in some cases, cuprase administered along with radium rays has been useful, and selenium and colloid gold have been suggested. It is possible that secondary radiations from substances locally deposited in the malignant cells might be locally engendered to the destruction of these cells. If it could be determined that malignant cells have a special affinity for some atom (the heavier the better) which is not shared by the normal tissues, an important step would be made. At present the gross method of locally injecting a tumour with such a substance as bismuth or silver is the only one that can be employed and is hardly to be commended.

Similarly, one cannot form an opinion as to whether treatment of malignant disease by way of the endocrine glands is practicable. There is no real line of demarcation between the non-malignant and the malignant growths on the one hand and the non-malignant growths and hyperplasias on the other. Hence the fact that irradiation of the thyroid greatly ameliorates the local and general condition in certain cases of exophthalmic goitre becomes of importance in the present connexion, particularly since irradiation leads to histological changes in the thyroid cells and colloid. Moreover, the fact that X-rays have recently been used with success in obesity may perhaps be compared with the influence of thyroid extract in the same direction. In acromegaly, too, it is stated that irradiation of the pituitary body has been followed by marked improvement in the symptoms. Lastly there is no doubt concerning the profound influence of rays upon uterine fibroids, whether the action be direct or by way of the ovary and an artificial menopause. Here may be recalled the relationship between cancer and the ovaries that was expressed in Beatson's operation of ovariotomy for cancer of the breast. From the examples that have been cited it is surely legitimate to argue somewhat after this fashion: if irradiation of an endocrine gland be followed by diminution in size of a hyperplasia or of a non-malignant tumour with which that gland is known to be intimately associated, is it not possible that, under some conditions of like kind, but as yet unknown, disappearance of malignant cells may be brought about?

Treatment by the mixed toxins of *Str. erysipelatis* and *B. prodigiosus*, particularly in the case of sarcomata of long bones, has again been the subject of a paper by Coley. He reports the results of 250 cases under his own care between 1890 and 1919. Of this series, in 15 cases of periosteal and 16 of central growth, life was prolonged well over 3 years, while in 17 of the 31 the limb was also saved. Nevertheless, in the majority of cases the toxin treatment was conjoined with amputation unless the growth was of the giant-cell variety. More recently, Coley has combined administration of mixed toxins with radium or X-ray treatment, and again, in these cases, amputation may or may not have been performed. There is no doubt that a great distinction obtains between the myeloma and the periosteal sarcoma in respect of malignancy, but even under the most severe criticism Coley's results remain far more favourable than those of surgeons in this country, and, indeed, more favourable than those of other American surgeons. The explanation of this is not clear, but it must be remembered that the beneficial effect of an attack of erysipelas in cases of malignant disease was asserted by many of the older surgeons. It may be that Coley owes a part of his success to the very belief he has in his line of treatment and the assiduity with which he carries it out. An attack of erysipelas would be simulated more closely if, instead of the toxins, a sensitized mixed vaccine were used; I do not know whether this modification has been tried, but *a priori* it seems reasonable. From an experimental point of view it is clearly undesirable to complicate the issue by combining treatment in this way with irradiation treatment.

But there is little doubt that the judgement of most competent authorities would be that, at the present time, treatment of malignant disease must proceed along the lines of a judicious combination of surgery and irradiation.

The treatment of cancer patients in those last stages when palliation alone is possible has not been the subject of publications. Incidental remarks as to the influence of radium and X-rays upon pain, haemorrhage, discharge, or fetor, however, are found, and there is universal agreement that benefit often results from their use. The diminution of pain after irradiation may be quite remarkable. In this connexion the experience of the Cancer Charity of the Middlesex Hospital is worth mentioning. It is that, by whatever means, the administration of morphia should be delayed to the utmost. It tends to superpose the morphia habit on the malignant disease, and thus to intensify the pain and mental anxiety of the patient and increase the difficulties of the nurse. Pain and sleeplessness can be effectually combated for a long time by means of aspirin, omnopon, and occasional irradiation.

Propaganda

It is obvious that improved results in cancer cases can be brought about by increased knowledge on the part of the medical practitioner. But he, in his turn, depends upon the patient. Careful examination of hospital records shows that, in spite of increased general knowledge, improved and cheaper means of transit, anaesthetics, and antiseptics, patients come to hospital for the first time with growths as large and as inoperable as they did fifty years ago. It therefore becomes a question whether public instruction on the subject of cancer is not desirable. The New York State Department of Health publishes a monthly bulletin called *Health News*, of which the February 1920 number is devoted to cancer. The pamphlet has been drawn up with very great care, but is popularly written, and the underlying object is to instruct the public sufficiently that they shall seek medical help as early in the disease as possible. Similar propaganda have been employed in Germany and France for some years and have been suggested in Great Britain. Clearly it would be necessary for provision of a sufficiency of hospital beds to run parallel with the propaganda. Otherwise the present evil of a long waiting list for admission might only be intensified.

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W. S. L.-B.

RENAL DISORDERS

Aetiology. In order to determine whether the elimination of abnormally large amounts of nitrogenous material by the kidney would causes nephritis, Newburgh, of Ann Arbor, fed rabbits with high protein diets and obtained the following results: (1) Renal injury was very quickly and constantly noted in rabbits that ate the whites of several eggs daily. (2) Prolonged feeding with white of egg caused acute and subacute nephritis. (3) When the nitrogenous metabolism was increased by means of casein, rabbits suffered no demonstrable renal injury from eating 15 grm. of casein daily; but when the daily intake of casein was 30 grm., and the nitrogen metabolism was about three times the normal, a well-marked deleterious effect upon the kidney was produced. (4) Rabbits that lived on soy beans for months regularly acquired chronic nephritis which was frequently fatal. The nitrogen metabolism from this diet was about twice the normal. (5) The renal lesion produced by high protein diet was not caused by the passage of too much urea through the kidney. These data suggest that the kidney injury was related to those digestive products of protein which vary both quantitatively and qualitatively with the type of protein eaten.

Hill, of the Boston Children's Clinique, believes that far more cases of acute nephritis in children are secondary to tonsillitis than to scarlet fever or any other acute infectious disease. He found that the nephritis did not usually appear during the period of sore throat and fever, but developed about a week after the patient had got up and was apparently well. In a series of 49 cases of acute nephritis in children, 25 were of a 'haemorrhagic' type, characterized by a large quantity of blood in the urine, and 24 of an 'exudative' type, characterized by marked oedema. In most of the 'haemorrhagic' cases tonsillitis was the aetiological agent, as it was also in the 'exudative' cases, but far more of the 'exudative' cases were of unknown aetiology than were cases of the 'haemorrhagic' type.

One case of acute nephritis secondary to middle ear infection is reported by Shuman in a girl aged 3½ years. After ligature of the external jugular vein and clearing out the lateral sinus the urine became normal, but a slight relapse occurred when the mastoid incision broke down.

A case of acute nephritis in a man aged 28, caused by absorption of household disinfectants (creolin followed by lysol) which had been applied to a wound in the foot, is recorded by Jones, who recommends that solutions containing coal tar should be made by being first thoroughly dissolved in cold water, enough warm water being added to bring it to the desired dilution, which should be of a very pale milk colour.

Symptomatology. Under the title of 'the meningeal mask of acute nephritis', Bonaba, of Montevideo, records two cases in children both aged 11 years in whom an attack of acute nephritis of unknown origin was ushered in by symptoms of meningitis. The cerebrospinal fluid, however, was normal, and examination of the urine showed casts and blood. Rapid improvement followed lumbar puncture, and recovery occurred in a few days. Why the intoxication should have affected the meninges in these two cases can only be explained by the assumption of a special predisposition without any more definite statement being possible.

At a discussion at the Berlin Urological Society on affections of the urinary organs caused by the war, Strauss remarked that the course of **war nephritis** was generally favourable, the mortality ranging from 0·7 to 3·3 per cent. More than three-quarters of the patients recovered more or less completely in the course of six to nine months, and only a small number of cases were converted into chronic nephritis. Uraemia and eclampsia occurred in only a few cases. The residual nitrogen in the blood at the height of the disease was usually increased to 50 to 100 mg., and as the condition subsided it fell to 60 or 40 mg. The blood-pressure in the initial stage was frequently raised, but in the latter stages was usually 130 to 140 mm. Hg. A reading of 180 mm. suggested a pre-existing chronic nephritis. Changes in the heart of any considerable degree were rare in the later stages. Albuminuric retinitis was found in 10 to 20 per cent. A tendency to relapses lasted for months and could be shown by resistance tests. As regards the portal of entry of infection, Strauss did not attach so much importance to tonsillitis or influenza as to pyodermia associated with vermin, and in support of his view alluded to the eosinophilia which was found in war nephritis as in dermatoses.

Heller, who was in charge of the renal department at Salzburg, between September 1917 and September 1918, states that during this period 408 cases of renal disease were under treatment, of which 206 or 50·1 per cent. were examples of chronic nephritis, 120 or 29·4 per cent. had relapses of acute nephritis, 80 or 19·6 per cent. had acute nephritis, and 2 or 0·5 per cent. had nephrosis. During this period 4 died, viz. two severe chronic cases from uraemia, and two during convulsive attacks with all the signs of pulmonary and cerebral oedema. Heller regards the prognosis of acute nephritis and of relapses as not unfavourable, as 25 per cent. of his cases were discharged in a fit condition to follow their occupation in civil life or even in the army. 50 per cent. of all the chronic cases were discharged with a diminished power of gaining their livelihood, but were able to carry on their work at home.

In his Paris thesis on the sequelae of war nephritis based on the study of patients admitted to hospital several months after the onset of the acute symptoms, Rouiller states that the predominating symptom was more or less marked pain in the lumbar region which was often accompanied by headache and general fatigue. Dyspnoea on exertion and slight visual disturbances such as *muscae volitantes* were fairly frequent. The signs, therefore, did not appreciably differ from those of nephritis seen in peace time. Examination of the urine showed slight albuminuria, microscopical haematuria, and casts The renal functions were generally sufficient. The amount of blood urea was generally about the normal, but modifications of Ambard's constant might be observed, and a slight rise of blood-pressure was not rare at this period. The prognosis should be guarded, as relapses are liable to occur. In this connexion, Gilow's description of his own case of relapsing haemorrhagic war nephritis may be quoted. He contracted nephritis in July 1918 after 42 months' front-line service on the Western front, and had a first relapse in August 1918, a second in January 1919, a third in September 1919, and a fourth in January 1920. There was nothing objective to show in the intervals, but he suffered from headache, pain in the back, and lassitude, so that he was unable to undertake a hospital appointment with its exacting day and night duty or to take up the life of a country doctor.

Schlayer writes on the end results of war nephritis in a paper based on the study of 191 cases, of which 135 were examples of pure war nephritis, i.e. acute nephritis which had developed at the Front without any recognizable cause, and 56 were the sequel of acute infections such as tonsillitis, dysentery, erysipelas, or paratyphoid. The onset of the nephritis dated back 48 months at most; in the majority of cases the disease was much more recent. Of the 135 true war nephritis cases, 6 or 4·4 per cent. ended in complete recovery after a period ranging from 5 to 31 months, thus showing that a war nephritis which has lasted a year should not necessarily be regarded as chronic. The most frequent result, however, was incomplete recovery with disturbance of function, which occurred in 67 cases or 49·6 per cent., after a period ranging from 1 to 4 years. In a large number of these cases an intercurrent attack of influenza gave rise to a relapse of acute haemorrhagic nephritis. Acute tonsillitis had a similar effect. But while the relapses due to influenza rapidly subsided without leaving any residues, an attack of tonsillitis often caused a permanent aggravation of the nephritis. 50 cases ended in complete recovery, with some disturbance of function, and 12 in contracted kidney. In 2 cases the occurrence or reappearance of oedema was found two years after the onset of the acute nephritis without any signs of cardiac involvement or any evidence of severe renal disease. The oedema was therefore due to the persistence of some extra-renal lesion, examples of which have already been recorded by Gerhardt (vide *Medical Science*, 1919, **1**, 270). Schlayer points out that the practical interest of these observations, lies principally in their prognostic significance. Although oedema in a renal patient is almost always regarded as a sign of severe renal disease, in these cases the oedema has very little prognostic significance and in most cases disappears without leaving any residues.

Howard and Robertson studied 37 cases of war nephritis, in most of which the onset had occurred four months previously. 19 were discharged as completely recovered, 9 presented the picture of chronic intestinal nephritis with one death from uraemia, and 9 still had nephritis but appeared to have a fair chance of ultimate recovery. Persistent albuminuria was common (64 per cent.), but in the absence of other signs of nephritis the patients were considered to have recovered. Polyuria was not uncommon, and was regarded as a valuable sign. In 5 out of 7 cases in which the 24-hour urine output exceeded 1,500 c.c. there was ample evidence of impaired renal function. Relative increase of night urine was practically constant in active cases and was not infrequently the only anomaly in those apparently recovered. Blood urea above 35 mg. per 100 c.c. usually meant nephritis, as was proved by other factors. Normal readings were frequently found in active cases. Moderate reductions of phenolphthalein output were not uncommon after apparent recovery. A high blood-pressure proved to be the most reliable single sign. Of 12 cases with a systolic pressure of 140 or more 10 had nephritis, and the other 2, in whom the maximum reading was just 140, showed no other signs of nephritis. On the other hand 6 of the 25 whose blood-pressure never reached 140 were nevertheless considered active cases. They were much milder, however, in type than the patients with higher readings and seemed likely to recover entirely. A moderate degree of anaemia was very common, the average red cell count being 4,147,500.

Tests of renal efficiency. Maclean and De Wesselow investigated the effects of war nephritis on kidney function, and came to the following conclusions: In the early stage of an acute attack of nephritis, the blood urea content furnishes the best indication of the state of the kidney. If this is normal, it may be taken for granted that the damage to the kidney is not sufficient to interfere with its normal function of excreting nitrogenous products. If on the other hand the blood urea is high, valuable information may be obtained as to the course of the disease. If the urea tends to get less, the prognosis is good; if it gets persistently higher, the prognosis is bad. In many subacute and chronic conditions the kidney is not sufficiently damaged to cause an increase in blood urea, and so no information can be obtained by this test. In such cases the capacity of the kidneys to concentrate urea in the urine affords very helpful information. If the urea concentration is low, it is in the great majority of cases an indication that the kidney is inefficient. The estimate of the diastatic index in conjunction with this test is of great value. Usually the indications given by both tests agree. In cases where functional tests indicate that the renal function is being efficiently carried out it is important to investigate the condition of the cardio-vascular system, for the indirect danger of cerebral haemorrhage or cardiac failure may be much greater than any direct manifestation arising from kidney inefficiency. As regards the phenolsulphonephthalein test the writers regard it as giving a very good indication of the state of kidney function in general, but as failing to differentiate between the different types of nephritis. When the kidneys are capable of secreting from 40 to 50 per cent. of this dye in one hour there is probably not much disturbance of function, but the test is not sufficient by itself to give the required information in the absence of other modes of investigation. In conjunction with other tests it is undoubtedly of much value.

According to Symes, tests of renal efficiency which include the water test, the specific gravity test, the test of the rate of secretion, the sodium chloride excretion test, and the estimation of the non-protein nitrogen in the blood are superior to the old tests for albuminuria, casts, &c., as they enable one to detect disease of the kidney at a much earlier stage.

Myers and Killian record their observations on 100 cases of nephritis showing creatinin retention. 85 of these had over 5 mg. creatinin per 100 c.c. of blood, and 80 of these died. Of the remaining 5 the condition remained unchanged in 3, and 2 in which there was only a temporary elevation of the blood creatinin recovered. The writers conclude that the test is of greater prognostic value than either the blood urea or phthalein tests which were used simultaneously, and believe that in advanced cases of nephritis the blood creatinin furnishes a more reliable prognosis than any other test.

Acidosis in nephritis. According to Chace and Myers of New York, all fatal cases of chronic nephritis with well-marked nitrogen retention show a severe acidosis, sufficient in many instances to be the cause of death. In some cases of acute nephritis and acute exacerbations of chronic nephritis the distress is apparently due to the acidosis, since the judicious use of sodium bicarbonate results in general clinical improvement. With the rise in the carbon dioxide power of the blood the dyspnoea and hyperpnoea disappear.

In view of the fact that Bornstein and Lippmann, in agreement with Martin Fisher, had stated that the albuminuria and cylindruria following severe exertion are caused by the increased urinary acidity, Barach, of the Presbyterian Hospital, Pittsburgh, examined a series of 57 normal young men, and found that in the most severe type of exertion (Marathon race) albuminuria, hyaline and granular casts, and red blood cells occurred in all cases. The largest amount of albumin, blood, and casts was found in those individuals with the greatest degree of circulatory disturbance, which was manifested by a marked fall in the maximum blood-pressure and in the pulse-pressure. In the less strenuous type of exertion an increased urinary acidity, albuminuria, casts, and at times blood cells were found. Urinary acidity was increased after exercise in 85 per cent., but it did not occur more frequently, nor was the acidity higher, in the cases of severe exertion than in the milder ones. Barach concludes that though a relationship exists between the degree of albuminuria and cylindruria and the type of physical exertion, no such relationship can be established between the urinary acidity and the occurrence of albumin, casts, and blood cells in the urine.

According to Roger, professor of neurology at the Marseilles Medical School, the **meningeal reactions** which occur in the course of uraemia do not appear to be directly caused by nitrogenous retention, but are the result of intercurrent cerebral complications, such as haemorrhage or softening. Renal sclerosis may be complicated by arterial hypertension, which may cause rupture of a cerebral vessel, and it is also partly responsible for the atheroma which leads to cerebral softening.

Under the title of **haemorrhagic recto-colitis of uraemic origin**, Bensaude, Cain, and Antoine, who record three illustrative cases, describe a condition which may develop insidiously or be manifested suddenly by very severe intestinal haemorrhage and dysenteriform diarrhoea. They recommend that the presence of blood in the stools of a patient with a high blood-pressure and suffering from chronic nephritis should prompt an examination of the rectum. In addition to the presence of haemorrhoids, which are so frequent in these patients, a careful investigation of the alimentary canal should be made, especially by rectoscopy, when the ulcerative lesions of haemorrhagic recto-colitis will often be found. The writers attribute the lesions to elimination of toxins through the intestinal mucous membrane and the haemorrhage to the high blood-pressure.

Barber has observed eight cases of **renal dwarfism**, amounting in some instances to true infantilism, associated with interstitial nephritis. Development was fairly normal until five or six years of age, after which growth was very much retarded. Bone deformities which occurred in five cases appeared to develop about the age of puberty. In type the changes appeared to be very similar to those of rickets. The wrists and knee-joints were most noticeably affected, but some swelling was palpable at the junction of the ribs and costal cartilages. Genu valgum was present in four cases.

According to Schemensky, of Frankfort, the first description of **nephritis without albuminuria** was given by Philipp, of Berlin, in 1840, who in an epidemic of scarlet fever found oedema to be a constant sequel, and in at least 60 of these cases noted an absence of albuminuria. Whether the examination made by him would have withstood criticism cannot be determined. Henoch, in 1873, described a *hydrops scarlatinosus* in which albuminuria was absent, though the autopsy showed the presence of nephritis. Until comparatively recently examples of nephritis without albuminuria had been reported only in children in relation to post-scarlatinal nephritis, but lately several instances have been recorded in adults. Thus, in the discussion on war nephritis at the Warsaw Congress in 1916, Neisser and Heimann distinguished three kinds of war nephritis, in the first of which, in spite of general or local oedema, the urine showed no pathological changes and complete recovery took place. In their opinion, these 'prenephritic phenomena' were due merely to hyperaemia of the kidney caused by vascular paralysis, the result of a long-continued vascular constriction. At the same congress Nonnenbruch also alluded to cases in which all the other symptoms of nephritis, including oedema and rise of blood-pressure, were present, but albumin was absent or found in only small quantities. Schemensky concludes that analbuminuric nephritis does exist, as is proved partly by the autopsy findings and partly by examination of the urinary sediment.

Fibrinuria. According to O'Conor, who records a personal case, and has collected 25 authentic examples from the literature between 1836 and 1913, spontaneous coagulation of the urine occurs very rarely without an admixture of blood or chyle. Its occurrence always indicates the presence of fibrinogen, and the resulting coagulum is composed of fibrin. The fundamental pathological condition in these cases appears to be a nephritis of varying grade and severity. In O'Conor's case, in which the fibrinuria was found in connexion with adenocarcinoma of the right kidney, the fibrin, as in the other cases on record, was not a product of the carcinoma itself, but a result of the associated renal destruction.

Lipuria. According to Bauman and Hansmann there are at least two types of lipuria, the one associated with a fistulous communication of the lymphatics with some part of the urinary system and the other due to an abnormal permeability of the renal cells. They record a fatal case of the second type in a man aged 37, in whom the clinical, chemical, and pathological findings indicated a progressive nephritis, possibly of syphilitic origin, associated with lipuria and terminating in uraemia.

Under the title of 'Urinary tract purpura, a probable entity', Stevens and Peters report a group of cases characterized by a purpuric condition confined in at least the majority of the cases entirely to the urinary tract. The condition was marked by an acute onset, irregular temperature, general febrile symptoms, frequent micturition, dysuria, gross haematuria, presence of casts, and a reduction of the phenolsulphonephthalein excretion. The disease appeared to run a prolonged subacute or chronic course. Occasionally acute relapses occurred. 26 definite cases and 11 doubtful cases were found in a period of 18 months in the British and American Expeditionary Forces, and constituted 14 per cent. of all the medical renal cases and 28 per cent. of the acute medical renal cases admitted to the hospital in a period of 10 months. Examination of the lesions obtained from the bladder wall by a cystoscopic punch showed submucous haemorrhages unaccompanied by any signs of inflammation. Bacteriological examination of the urine and blood proved negative, and attempts to determine the aetiology of the condition or to identify it with any known disease were unsuccessful.

Pfister, of Dresden, emphasizes the value of albuminuria produced by renal palpation in the diagnosis of **movable kidney**. In such cases the urine should be examined before and after palpation. He records a case in a soldier who, as the result of being buried by an explosion, developed a swelling in the right hypochondriac region. Gall-bladder disease was at first suggested, but subsequently the diagnosis of movable kidney was made and was confirmed by examination of the urine, which before palpation was completely free of albumin, and after examination showed traces of albumin and a few red cells. On another occasion slight massage of the kidney was performed, and the urine, which had previously been quite normal, showed a marked turbidity, an albumin content of 2·1 per mille (Esbach), numerous granular, hyaline, and blood casts, and red and white corpuscles—in other words, all the signs of a right-sided traumatic nephritis. As on the first occasion, the urine became normal the next day and remained so.

A case of severe local and general disturbances due to **oxaluria** is recorded by Motzfeldt (1). The patient was a nurse, aged 28, who had been troubled since childhood by frequency of micturition and occasionally by incontinence. She was tired and nervous, and complained of 'rheumatic' pains in the back and ankles. In 1914 the frequency of micturition was accompanied by occasional attacks of pain in the lower abdomen. The suspicion that she suffered from renal calculus appeared to be confirmed by the passage of a small stone, after which the pain ceased for a time. There was no haematuria. The bladder symptoms were most distressing when she felt overworked, and caused least discomfort when she had a holiday. Irrigation with silver nitrate gave no relief. By the summer of 1918 she had become practically incapacitated for work by the bladder symptoms. She had to micturate at least every hour, and even so she could not keep dry. She had to get up twice every night to micturate, and she became very depressed and nervous. She was first seen by Motzfeldt in the autumn of 1918, when an examination of the clear and normal-looking urine failed to reveal any pus or albumin. But when the urine was centrifugalized and the sediment examined under the microscope, numerous typical oxalate crystals were found. They were demonstrable even in recently passed warm urine. An oxalate-free diet (no tea, cocoa, vegetables, or fruit), and alkalis, given by the mouth, were prescribed, and milk and eggs were interdicted on account of their high calcium content. In a week she was much better, and the bladder symptoms had almost vanished. The effectiveness of this treatment was further demonstrated by a relapse when she returned to a normal diet for a week. The symptoms vanished two days after she had resumed her dieting. Examined in March 1919, she was found to be perfectly fit, and she could dispense with alkaline drugs. But the bladder symptoms were apt to recur even after the drinking of a couple of glasses of milk. Motzfeldt suggests that it is rare for oxaluria to induce such severe local and general disturbances. The latter coincide so closely with those of neurasthenia that, unless the sediment in the urine is microscoped, the real cause of all the symptoms is apt to be overlooked.

Cystic inflammation of the renal pelvis, ureter and bladder is discussed by Jacobson, of the Wisconsin Medical School, who describes it as follows: It is primarily a disease of old age, 95 per cent. of the cases occurring in senile arteriosclerotic individuals of either sex, from whom a previous history of urinary inflammation or other disturbance can be obtained. The cysts arise from degeneration of the living epithelium, particularly that which has become cut off from the surface of the mucosa forming the "cell nests" of von Brunn. In view of the large number of these cell nests in the ureter and bladder of senile individuals and the high incidence of infections of the urinary tract in the aged, Jacobson believes that the incidence is much commoner than the literature would indicate. He records three examples in men aged 66, 74, and 83 respectively, two of whom had a history of prostatic trouble and the third bilateral pelvic calculi. In one a double ureter was present, the occurrence of which has been noted in several of the other cases on record.

Prognosis. According to Symes, the outlook with simple chloride retention is good, even if uraemic symptoms be present, whilst that of nitrogen retention with uraemia is much graver. In secondary sclerotic nephritis, if the patient escapes the dangers of uraemia he is most likely to succumb to cardiac failure, if he is a man below 50 years of age, whilst at any later period cerebral haemorrhage is most to be feared.

Henes, in 1915, showed that a hypercholesterinaemia was present in all cases of chronic nephritis, and that the cholesterinaemia decreased as the uraemic state was approached. He now records 12 illustrative cases of the prognostic value of cholesterinaemia in chronic nephritis, and quotes several authorities in defence of his belief that cholesterol plays some protective rôle in the animal organism.

Treatment. The main principles of dietetic treatment according to Symes are as follows: (1) When renal efficiency is low, and nitrogen is retained, the intake of nitrogenous food must be limited and plenty of fluid allowed. (2) When there is general oedema and the chloride elimination is low, the supply of salt must be cut off, and the allowance of water diminished. Symes thinks that a successful cure of chronic parenchymatous nephritis is much more likely to follow the procedure suggested by Epstein, than the use of diuretics. The loss of large quantities of albumin in this form of nephritis causes a decrease in the osmotic power of the blood, thereby favouring absorption and retention of fluid by the tissues. The blood in such cases shows a marked decrease in protein and increase in fatty bodies (lipoids). The indications for treatment, therefore, are first to increase the protein content of the blood, and thus restore its osmotic power, and secondly to remove the excessive lipoids. This is effected by administering a diet rich in protein and poor in fat, such as fish, lean meat, lean ham, white of egg, oysters, lentils, peas, rice, oatmeal, bananas, skimmed milk, coffee, tea, and cocoa. Starchy foods are limited to promote the maximum assimilation of proteins, and to lessen the retention of water. Fat is limited to lessen the amount of lipoids. Symes has found that this diet is not only most efficacious in reducing nephritic oedema, but also results in a very marked improvement in the patient's general condition, and reduces the amount of albumin in the urine.

A case of chronic renal dropsy successfully treated by Epstein's diet is also reported by Box, who maintains that this diet affords slow and steady relief to the dropsical symptoms in chronic nephritis of the hydraemic type, though he admits that the ultimate outcome is still *sub judice.*

After giving a general review of the dietetic treatment of renal insufficiency since 1831, Motzfeldt (2) gives his own views, partly illustrated by reports of cases. One of these was most striking. A young man with acute nephritis was given a salt-free diet, which in 22 days relieved him of his oedema and reduced his weight by 27 kilos, the output of chlorides exceeding the intake by 250 grm. Several charts are reproduced, showing the effect of a low protein diet on the urea content of the blood and the phenolsulphonephthalein output, as compared with the protein content of the food. Motzfeldt concludes that neither a strict salt-free nor a strict low protein diet can be achieved by milk alone, although a milk diet has been recommended in nephritis for nearly a century.

As the result of a rapid improvement in a case of uraemia following an abscess due to infected scarification wounds, Lemoine, of Lille, recommends fixation abscess as treatment for every case of uraemia not improved by the usual methods. He remarks that this is not the first example of a good result obtained by a fixation abscess in other affections than infectious disease. He has employed the method in cases of lead poisoning with almost invariable success. Arnozan has also derived benefit from its use in cases of poisoning by carbon monoxide, carbolic acid, and oxalic acid.

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J. D. R.
C. L.

MUMPS

Bacteriology. Haden reports five cases of mumps in which a Gram-positive diplococcus was isolated from the spinal fluid, the blood, and a lymph gland. The injection of the organism into the testicle of a rabbit produced severe orchitis in ten days. He concludes that mumps is probably caused by a Gram-positive diplococcus and not by a filterable virus according to the view recently prevalent.

Pathology. As the result of their comparative studies of the saliva in health and in mumps, De la Prade and Loiret (1), (2) found that the cytology and physio-pathology of the submaxillary and parotid glands in mumps were much the same as in the normal state. Catheterization of the salivary ducts showed that there was no important difference in the character of the cells exfoliated, or in the fermentative activity of the saliva, or in the quantity of the secretion. These observations indicate that the inflammatory reaction caused by the specific agent of mumps must take place almost exclusively in the peritubular connective tissue without affecting the glandular elements—a conclusion which corresponds with the present state of our knowledge of the morbid anatomy of mumps.

Symptomatology. Macleod records his observations on 694 cases of mumps in adult males aged from 18–40, 78 per cent. of whom were Australian troops. The parotids were usually first affected; in 64 per cent. the left parotid was the first involved. In 17 per cent. the disease was confined to the left side; in 20 per cent. the right side alone was affected, and in the remainder both sides were ultimately implicated. In 9 cases orchitis was the first manifestation; 4 of these had no glandular involvement, 2 others had pain only in the lower jaws, and the remaining 3 developed parotitis 3 or 4 days after the onset of orchitis.

Orchitis, which was the most frequent complication, occurred in 140 or 20 per cent. usually about the seventh day, but 16 developed it after the tenth day. In 16 per cent. both testes were affected. Symptoms suggestive of pancreatitis, such as fever, headache, vomiting, and pain and tenderness round the umbilicus, occurred in six cases. There was considerable rigidity of the left rectus, but no tumour was felt, and there was no evidence of undigested fat in the stools. Other complications were bronchitis, tonsillitis, rheumatism, and conjunctivitis; laryngitis and aphonia occurred in 8 cases; earache and deafness in 3, diarrhoea in 2, and in 2 suppuration of the parotid. In 2 death was due to intercurrent disease. Relapses occurred in 17 cases. In 8 the parotid was involved, in 8 the submaxillary, and in 1 the sublingual. The relapses occurred from the 10th to the 30th day, and always at a distinct interval after subsidence of the primary swelling.

Bardachzi and Barabas report their observations on an epidemic of 52 cases of mumps which occurred in the Przemysl garrison. 45·6 per cent. were under 20 years of age, and only 4·3 per cent. over 40. In 11 per cent. the affection was exclusively right-sided, in 14 per cent. left-sided only, and in 75 per cent. bilateral. Orchitis occurred in 10·8 per cent. This comparatively low figure the writers attribute to the impairment of the sexual function caused by the war. A case was observed of primary orchitis followed four days later by parotitis. Among the rare complications observed were 1 case of otitis media and 1 of pleurisy. One patient gave a history of having had an attack of mumps one year previously, and in another case a relapse was observed four weeks after the primary attack. The average period that a patient was kept in hospital was three to four weeks, so as to prevent fresh infections and complications.

Howard reports three cases of meningo-encephalitis as the only manifestation of mumps in soldiers, aged 21, 25, and 29 years respectively. The reasons for regarding the cases as examples of mumps in spite of the absence of inflammation of the salivary glands were as follows: (1) They occurred during a mumps epidemic; (2) two of the patients had never had mumps; (3) they all presented mild symptoms of meningo-encephalitis which were entirely relieved or much improved by lumbar puncture; (4) in two of the three cases a Gram-positive diplococcus, which is regarded by Haden as the cause of mumps (*vide supra*), was recovered from the spinal fluid; (5) the spinal fluid in each case presented a moderate pleocytosis characterized by a predominance of the mononuclear cells. The other conditions with this cytological picture could be excluded, namely, syphilis, except in one case which had a positive Wassermann reaction, tuberculosis, meningitis, and encephalitis lethargica. In the case with the positive Wassermann reaction a Gram-positive coccus was repeatedly found in the cerebrospinal fluid, so that some infection besides syphilis must have been present.

According to Rompe few cases of neuritis following mumps have been recorded. All forms of the disease including complete reaction of degeneration may occur. Most frequently the condition is a polyneuritis, chiefly affecting the extremities. The facial, optic, and auditory nerves may also be affected. The prognosis is favourable as regards polyneuritis and neuritis of the auditory nerve, but unfavourable in cases of involvement of the facial and optic nerves, especially when suppuration of the parotid occurs.

Margarot made a systematic examination of the oculo-cardiac reflex in soldiers in all stages of mumps. The cases were mild or of moderate intensity, and severe attacks were exceptional. During the acute stage ocular pressure caused a considerable slowing of the heart-beat in an unusually large number of cases. The diminution in the pulse-rate was not only more frequent but more marked than usual, and in 5 cases ocular pressure caused an actual stoppage of the heart for a few moments. Another interesting observation was that when once the test was decidedly positive, spontaneous bradycardia occurred the next day or the day following. When the reflex was positive but not exaggerated, the onset of bradycardia was less sudden but progressive. The diminution in the number of cardiac contractions was accompanied by a fall of blood-pressure, the action of the vagus being at once inhibitive and hypotensive. Hypertonus of the vagus is therefore definitely present during the acute stage of mumps. The oculo-cardiac reflex is definitely positive throughout the course of the disease, but it may undergo certain variations. In convalescence, ocular pressure has a less marked effect than before. In some cases even the reflex becomes abolished or even inverted. If a complication occurs, the normal bradycardia of convalescence is replaced by acceleration of the heart's action and the reflex, though usually remaining positive, is rarely exaggerated. In 3 of Margarot's cases it became negative. In the case of pancreatitis with pressure of the enlarged gland on the solar or coeliac plexus the sympathetic tonus momentarily becomes more marked and the reflex is inverted.

According to Margarot the constant overaction of the vagus in mumps may be attributed to an attenuated meningeal reaction with direct stimulation of the vagus centres, or to a reflex stimulation of these centres by a peripheral irritation in the salivary glands, testes, or lymphoid tissue.

Ruge records a case of mumps in a woman complicated by haematoma of the left ovary. The symptoms subsided without operation.

Three cases of **pseudo-mumps** or chronic parotitis in soldiers exactly similar to those described by Mattei (vide *Medical Supplement*, 1918, **1**, 253 *b*) are reported by Dénéchau. In none of the cases was there any evidence of plumbism, malaria, tuberculosis, or syphilis, nor did the condition appear to be due to malingering as in the case recorded by Trémolières and Caussade (*ibid.*, 1918, **1**, 340 *b*). Mallié of Bordeaux, and Blumenthal of Coblentz also report similar cases in soldiers. Mallié states that on examination of the bucco-pharyngeal cavity some source of infection was frequently found, such as gingivitis, stomatitis, or tonsillitis. There was no general disturbance, and the disease was completely apyrexial. Unlike mumps, there was no contagion and no complications. Blumenthal found it impossible to say whether the condition was due to an ascending inflammatory process owing to defective oral hygiene in the field, or to a true hypertrophy of the glands caused by munching coarse food.

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J. D. R.

SMALL-POX

Aetiology. According to Sobernheim, of Berne, the virus of small-pox, even at an early stage of the disease, is present in the mucous membrane of the upper respiratory tract, and there can hardly be any doubt that transmission of the disease occurs by droplet infection. This is the only means of explaining why small-pox is so infectious at an early stage before the appearance of the eruption. The old variolation experiments showed that the course of the infection by the skin was remarkably different from naturally acquired small-pox as regards the incubation period, the localization of the eruption and the severity of the disease. The difference in the course of inoculated and natural small-pox is incompatible with a belief in the same mode of infection.

Epidemiology. According to King the total data available point to the existence of grades of virulence of small-pox recognizable as two types (Eastern and South African), two strains (Western and South African or Amaas), and one substrain (Western). (1) The 'Eastern type', which is the most virulent form of small-pox, is found east of long. 40° E. and between lat. 40° N. and 6° S. Among Asiatic populations the general fatality rate per cent. ranges from 33 to 50; in the vaccinated of all ages from 30 to 60, and in the unvaccinated from 60 to 80. (2) To the west of long. 40° E. the Eastern type loses much of its virulence and forms a 'Western strain' capable of (but very rarely) reverting to the virulence of the parent stock. The general fatality in pre-vaccination days from this strain was from 18 to 25, and since then in the vaccinated from 1 to 5 and rarely over 7 per cent.; in the unvaccinated from 19·3 to 47 per. cent. (3) In certain European countries including Great Britain, France, Germany, Belgium, Holland, Switzerland, Denmark, Norway, and Sweden the general fatality rate is so much smaller than in any part of the world where either the Eastern type or its Western strain is evident as to justify the recognition of a 'Western substrain' of small-pox. (4) In South Africa there is a second type of small-pox known as the 'Amaas type', which is distinguishable from the Eastern type and its Western strain by its mild constitutional symptoms, though it is attended with considerable skin disturbances. The general case fatality is from 3·8 to 4·3 per cent. This source has probably given rise to a strain of less virulence ('Amaas strain') which has appeared in races of European origin in America, Canada, and Australia. In the former two countries the fatality rate is about 1·8 per cent., and in the latter less than 1 per mille.

In a paper on the spread of small-pox in Germany and Austria since the outbreak of war, Gins, who is superintendent of the State Vaccination Institute in Berlin, states that during the first two years of the war Germany was almost free from small-pox. In the spring of 1916 a slight rise in the number of cases occurred. A further increase in June, July, and August was to be attributed to the Wolhynian refugees (vide *Medical Supplement*, 1918, **1**, 94). After the number of cases had sunk down to the peace level in autumn, another outbreak occurred in December, in Schleswig, and from this region cases spread over a large part of North Germany and the South German states. In 1917 there were 2,300 cases of small-pox in Germany, nearly all of which occurred during the first half of the year. There were

500 cases in Berlin. From January to November inclusive 1918 was like a peace year as regards small-pox. In December a fresh outbreak took place, chiefly involving Saxony, Silesia, and East and West Prussia, and giving rise to 1,300 cases during the first three months of 1919. In 1914 Austria-Hungary was as free from small-pox as Germany until the war began. During the first six months of 1914 only 154 cases were notified, but towards the end of the year there was an increase in the number of cases, 306 cases being notified in the last quarter. In the spring of 1915 an epidemic began; 4,855 cases occurred in the first half, and 18,647 in the second half of 1915. The epidemic increased in the first six months of 1916, there being 18,499 cases in the first six months. In the second half year the cases dropped down to 489, but in 1917 there was another rise, 1,378 cases being notified in the first six months. No figures were available for the second half of 1917 or for 1918. After the downfall of the Austro-Hungarian Empire 113 cases were notified in German Austria from October to December 1918, and 191 from January to March 1919.

Sobernheim states that the epidemic in Germany at the end of 1916 and in the first half of 1917 was relatively mild, the mortality being about 10 per cent. Elderly persons chiefly were attacked who had not been vaccinated for from 10 to 20 years. In Berlin 80 per cent. of all the cases were over 40, and the attack was generally of the varioloid type, though a few cases of haemorrhagic small-pox occurred.

The efficacy of vaccination in the case of the German army during the war is emphasized by Sobernheim, who states that when German troops invaded the districts of Poland in which small-pox was rampant, they were practically unaffected by the disease, although they remained there for months, and personal hygiene was quite out of the question, their immunity being due to revaccination on enlistment and again at the commencement of the war. The defective vaccination of the Polish population was shown not only by the large number of small-pox cases, but also by the predominance of the disease in children. Its distribution among the various classes of the Polish population was also very instructive. The Jews who had had their children vaccinated in infancy were little affected by small-pox, while the Poles who had neglected vaccination suffered severely. That it was only the performance of vaccination which accounted for the difference in the distribution of small-pox was shown by comparison with other infectious diseases. The Jews were most unfavourably situated as regards their housing and mode of life, and were attacked by other contagious diseases such as typhoid and typhus to a far greater extent than the rest of the population.

According to Soucek small-pox was very prevalent in Vienna in 1915, when there were 1,566 cases, of which 350, or 22 per cent., were fatal. The first year of life was represented by 100 cases, the fourth by 108, and the first to fifth years by 461. The number then diminished up to 14, in which year there were only 10 cases, and then rose again to 150 between 36 and 40, when it slowly fell again. The mortality was very high in early life, viz. 73 per cent. in the first year, 40 per cent. in the second year, 43 per cent. in the third year, and 46 per cent. in the first to fifth years. The mortality, like the morbidity, sank up to the age of 14 and 15 when it was 0 and 5 per cent. respectively, and then gradually rose up to 20 per cent. between 51 and 55 and to 50 per cent. in persons over 70. Of 100 cases in the first year of life only 1 had been successfully vaccinated, 57 had not been vaccinated at all, 39 had been vaccinated less than 3 weeks before their attack, and in 3 the result of vaccination was not known, but was probably unsuccessful. Of the unvaccinated 46 died, of those vaccinated too late 24, and also the one vaccinated case. Of the total 1,566 cases only 34 had been vaccinated or revaccinated within the last six years, and of the 350 fatal cases only 2 had been successfully vaccinated. The Vienna small-pox epidemic of 1915 therefore showed an almost exclusive incidence among the unvaccinated or those who were no longer sufficiently protected by vaccination. In the total number there were only 2·1 per cent., and among the fatal cases only 0·57 per cent. who ought still to have been fully protected by vaccination.

Two of the cases had already had an attack of small-pox. In spite of the highly contagious character of small-pox, the epidemic remained fairly small compared with those of other diseases. Thus, during the same year in Vienna, there were 5,212 scarlet fever cases with 563 deaths, 2,181 dysentery cases with 75 deaths, and 2,869 typhoid cases with 563 deaths.

Johnstone describes an outbreak of small-pox in occupied Germany which was traced to a Polish soldier who had recently been demobilized from the German army. Owing to the British military authorities insisting on a rigorous isolation of patients and contacts and the general vaccination of the inhabitants the area of infection was limited. There were in all 30 cases, 4 of which died, 3 of the 4 belonging to the nursing staff of the hospital. The susceptibility of the aged to the disease is shown by the fact that 8 or about two-thirds of the occupants of an almshouse contracted small-pox, 5 of them being aged from 70–81.

Fasquelle, who was director of the anti-small-pox service of the French army during the war, states that whereas in 1870–1, 125,000 French soldiers at least contracted small-pox with 23,470 deaths, and more than 18,000 deaths occurred among 200,000 cases in Paris alone, this is the first time in history that a war has not been accompanied by an epidemic of small-pox. During the last two years of the war a few cases of small-pox, chiefly introduced from abroad, had occurred in certain departments and even in Paris, but the French army as a whole, exclusive of the Colonial troops, had only 12 cases during the four years of the war with one death. There were in addition 44 cases with four deaths among the Colonial troops. Fasquelle attributes this magnificent result to the laws of 1902 and 1915 on compulsory vaccination and revaccination, the free distribution of active lymph throughout France, and the vigorous measures employed in the army, including compulsory revaccination of all officers, among whom the incidence of small-pox used to be higher than among privates.

In a paper read before the Académie de Médecine on June 24, 1919, Wurtz stated that though small-pox was practically non-existent in Paris and the suburbs during the war there had recently been an increasing number of cases, as was shown by the following figures:

1914 (August to December) . .	6 cases
1915	7 ,,
1916	4 ,,
1917	6 ,,
1918	55 ,,
1919 (first five months) . . .	47 ,,

He attributed the spread of the disease partly to the introduction of cases from abroad, viz. from Morocco, Spain, Italy, and Algeria, and partly to the neglect of vaccination and especially revaccination by the public. Women and elderly persons were the chief offenders. In Wurtz's statistics the great majority of cases occurred in women. In an almshouse, of which he was the medical officer, more than 60 per cent. of the inmates had refused to be revaccinated.

Reece points out that several outbreaks in England and Wales in 1918–19 were referable to the fact that the original case of imported small-pox had occurred in a vaccinated soldier or civilian in whom the constitutional disturbance and amount of rash were so slight as easily to escape recognition. This was especially likely to occur in soldiers returning from the Eastern theatres of war, many of whom were liable to regard their illness as due to malaria and not seek medical advice till the true nature of their disease became known through the occurrence of several cases of small-pox in their homes.

Diagnosis. Sobernheim regards the method described by Paul in 1914 as indispensable for the diagnosis of small-pox. All observers are agreed that a positive reaction is a proof of small-pox, though a negative result, as is often the case in biological diagnosis, is not conclusive. The method consists in inoculating the contents of the suspicious pustule into the cornea of a rabbit and examining the result in 36 to 48 hours' time. If the case is one of small-pox, the cornea in the neighbourhood of the inoculation remains clear, and only shows fine nodules at the actual site of inoculation. These can be recognized with the aid of a hand-glass, but are seen more distinctly after killing the animal, enucleating the eyeball and placing it for a short time in sublimate alcohol. The cornea at once assumes an opaque grey appearance from which the nodules stand out as chalky-white isolated or confluent lesions. This characteristic appearance is only found on inoculation of small-pox or vaccine virus.

Loederich and Bory investigated the Wassermann reaction in four cases of small-pox. Three of these were in negroes who showed positive reactions with all antigens during and after their attack, so that they were probably suffering from syphilis or from some allied exotic affection. The fourth case was in a non-syphilitic Frenchman, who showed a positive reaction on the fifth day of a discrete attack with Desmoulières' antigen, and a negative reaction with all the others. On the thirty-first day the reaction was negative with all antigens.

Treatment. The local application of a solution of potassium permanganate which was first recommended by Dreyer of Cairo in 1910 is advocated by Bender of Breslau, who regards it as superior to every other form of treatment of small-pox. On admission to hospital the whole body is painted over with a freshly prepared saturated solution of potassium permanganate. Every following day, according to the sensitiveness of the skin the same solution or a 1·5 per cent. solution is used, and in persons with very sensitive skins a weaker solution still. It is claimed that this treatment prevents complications, septic fever, extensive bed-sores, purulent metastases and general sepsis, and shortens convalescence. Lastly, owing to the lesser amount of suppuration, smaller scars may be expected.

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J. D. R.

MEASLES

Bacteriology. On examination of a group of measles cases occurring a few weeks after an epidemic of influenza Sellards and Sturm found an organism indistinguishable from the Pfeiffer bacillus in 25 out of 31 cases. The organism was obtained readily from the sputum and with little difficulty from the conjunctiva, but was not found in the blood-stream or in excised skin lesions. On subsidence of the active symptoms of measles the micro-organisms disappeared rather rapidly in about three-quarters of the cases. Inoculation of the Pfeiffer organism from cases of measles on the mucous membranes of four healthy volunteers, two of whom were supposed not to have had measles or influenza, proved negative. The writers conclude that the occurrence of Pfeiffer's bacillus both in measles and influenza is evidence against its aetiological relationship in either disease. On the other hand, they point out that its specific aetiological rôle in some of the acute respiratory diseases cannot be entirely excluded.

From examination of the throats of 458 cases of measles, 48 of which were complicated by broncho-pneumonia and 43 by otitis media, Knowlton found that there was no relation between the presence of haemolytic streptococci in the throat and the occurrence of these complications, the percentage of these organisms being about the same in the complicated cases as in the total number.

Inoculation. (*a*) In man. Sellards (1) alludes to the two cases reported by Hektoen in 1905 in which measles was successfully inoculated by subcutaneous injection of measles blood taken during the eruptive stage, a mild but typical attack developing after an incubation period of about a fortnight. Sellards himself recently inoculated eight apparently susceptible individuals in various ways, viz., subcutaneously, intramuscularly, intravenously, and on the mucous membranes with blood or mucous secretions from patients in the eruptive or pre-eruptive stage, but none developed the disease. He points out, however, that failure to transmit the disease does not necessarily exclude the possibility of the occurrence of the measles virus in the circulating blood. The possibility of active immunity having been produced by inoculation was suggested by exposure to natural infection of measles failing to produce the disease. (*b*) In monkeys. Sellards (2) also injected blood from two early cases of measles in the pre-eruptive stage subcutaneously or intraperitoneally into 2 monkeys (*Macacus rhesus*). One animal remained free from symptoms; the other developed a moderate leucopenia and later a slight rash. A portion of the same specimen of measles blood was injected subcutaneously and intramuscularly into two human volunteers without any symptoms resulting. A specimen of blood from the monkey which subsequently developed a rash was injected into a susceptible volunteer, but produced no symptoms. Normal serum injected into monkeys was followed by a very slight erythema appearing about 8–10 days after injection in four out of ten animals. Sellards concludes that the weight of evidence is against the symptoms in the monkey being interpreted as a reaction to the virus of measles.

Commenting on Sellards's first communication Nicolle and Conseil allude to their experiments in 1911 and 1913 in which they successfully inoculated a monkey with blood taken from a measles patient in the acute stage and with the blood of this monkey passed on the disease to two other monkeys and a child, and lastly with the blood of the second child obtained a positive reaction in two other monkeys and a negative reaction in one. Nicolle and Conseil conclude that the blood in measles should be regarded as virulent, and attribute Sellards's negative results to his having experimented on individuals who had probably already had an abortive attack of measles.

Epidemiology. Brownlee reports an epidemic in a Highland glen from which measles had been absent for more than 80 years. Though the soil was practically virgin, and hardly any one escaped the disease, not a single death occurred.

Friedjung of Vienna records five examples of the immunity of breast-fed infants to measles in spite of the absence of isolation in families where the disease was prevalent during an extensive epidemic in Vienna in the spring of 1918. He adds, however, that he had seen numerous cases of measles among breast-fed as well as in bottle-fed children during the same epidemic, so that the rule as to the immunity of breast-fed children to infectious diseases in general and measles in particular is by no means of universal application.

Symptomatology. O'Shea reports a case of *haemorrhagic measles* in a boy aged 5 years characterized by extensive cutaneous haemorrhages resembling scurvy or purpura, severe haemoptysis, subconjunctival haemorrhages and signs suggesting haemorrhagic pericardial effusion, associated with a comatose state. Contrary to the general rule in such cases the patient recovered.

Berg of the Willard Parker Hospital, New York distinguishes haemorrhagic measles, which is an extremely fatal disease characterized by haemorrhages from the mucous membranes and toxic cerebral symptoms, from hyperpigmented measles, in which the prognosis is very much better than in ordinary measles. In hyperpigmented measles the eruption is much more brilliantly red than in ordinary measles, does not fade on pressure, and retains its brilliant colour up to the seventh or eight day before it begins to fade. The desquamation stage is delayed, and when it begins the scales are larger and coarser than in ordinary measles. There are no extravasations of blood under the skin or mucous membranes.

In a paper on the *intestinal complications* of measles Funaioli states that during several years' residence at Tripoli where there is a more or less extensive epidemic of measles almost every year, he observed 185 cases of measles and paid special attention to the intestinal symptoms. In 16 cases, or 8·64 per cent., they occurred before the eruption; in 45 cases, or 24·32 per cent., during the eruption, and in 43 cases or 23·24 per cent., of which 12 were fatal, as the rash was fading. These figures are much lower than those of Scherer who had a percentage of 38·70 of enteritis cases during the eruptive period with a mortality of 16·66 per cent. Probably the difference was due to the severity of the measles infection. On the other hand, Scherer had only 3·54 per cent. of enteritis cases in the prodromal period. Funaioli therefore classifies the intestinal disturbances of measles into prodromal, concomitant or primary, and secondary. The primary he regards as undoubtedly due to the measles virus and the intestinal enanthem, and the secondary to the ordinary bacteria inhabiting the intestine, the desquamation of the epithelium following measles depriving the intestine of its normal means of defence. The intestinal phenomena of the prodromal period are to be considered as a coincidence or as an exacerbation of a pre-existing enteritis, because the measles virus cannot then have produced any considerable lesions in the intestine.

Neff reports a fatal case of bullous eruption complicating measles in a girl aged 6. The bullae began to come out in the first twenty-four hours of the measles rash and appeared in various parts of the body, accompanying the measles eruption but never preceding it. The measles eruption was not more pronounced than usual, but the lesions persisted and the colour became darker and bluish. No petechiae appeared. The temperature remained high throughout. Pneumonia was possibly present, but respiratory symptoms were not prominent, physical examination of the chest was impossible owing to the raw surfaces, and a necropsy was refused. Other cases of a bullous eruption preceding, accompanying, or following the measles eruption have been reported by Steiner, Henoch, Baginsky, Leiner, and others, but the complication is very rare. Neff suggests that the secondary infection of this type is due to the lowered resistance occurring in measles.

Blood. Schiff and Mátyás (1) investigated the number of red cells and haemoglobin content in 27 cases of measles with the following results: In the prodromal stage before the appearance of the eruption and in many cases at the beginning of the eruptive period there was a pronounced fall in the red cell count. The haemoglobin content at the beginning of the disease was more or less diminished and did not show any obvious change on diminution of the red cell count. In a certain number of cases the haemoglobin content showed a rise and in others it remained on the whole unaffected. Complications did not appear to have any effect either on the haemoglobin content or the red cell count. The changes were thus almost the same as those which the writers had found in the cases of scarlet fever with the following difference: whereas in scarlet fever there was usually a pronounced fall in the number of red cells on subsidence of the acute symptoms, in measles during the eruptive period there was no change in the normal red cell count, the diminution in the red cells having usually occurred in the prodromal stage.

Schiff and Mátyás (2) also investigated the number of blood-platelets and coagulation of the blood in 18 cases of measles. In most cases their number was diminished on appearance of the eruption or of Koplik's spots, and an increase occurred as the rash faded. The severity of the disease did not seem to affect the number of the blood-platelets. The bleeding time was usually shortened. The coagulation time ranged from one to five minutes, and varied considerably in the same child. Retractility of the clot was always normal.

Loederich and Bory investigated the *Wassermann reaction* in 13 cases of measles with the following results. With Desmoulières' antigen the reaction was positive in 10, doubtful in 2, and negative in 1. With other antigens the reaction was negative in all but 1 case. In most of the cases the reaction was very transient, for it was negative by the 13th or 15th day; in only two cases was it still positive on the 16th and 19th days. The writers were unable to follow up these two patients, who may possibly have had latent syphilis.

Diagnosis. For administrative purposes Brownlee considers that only two symptoms are of the slightest use in the early diagnosis of measles, viz. evening rise of temperature and oedema of the palpebral conjunctiva, especially of the lower lid. By the time Koplik's spots have appeared, the mischief is done.

Regan points out that Fordyce's disease is apt to be mistaken for Koplik's spots, especially when it occurs in patients with German measles. The condition which was described by Fordyce in 1896 is a chronic disease of the mucous membrane of the mouth and lips characterized by the presence of whitish and yellowish lesions ranging in size from a pin-point to a pin's head, and chiefly found on the buccal mucous membrane along the line of the teeth as far back as the last molar. It is most common between the ages of 20 and 40. Well-marked cases of Fordyce's disease are unusual in young children. Slight cases, however, are frequent, but the lesions are so small and few, and often situated so far back on the mucous membrane or so nearly the normal colour of the buccal mucosa, as usually to be overlooked unless a careful search is being made for Koplik's spots.

Prophylaxis. Brownlee considers that a very large proportion of children under 5 years who take measles are infected by elder brothers or sisters who are attending school. As very few children develop the first symptoms of measles within the first seven days of infection, he maintains that no harm will ensue if the child stays at home for seven days after exposure, but he suggests that during the next seven days it should stay with its grandmother or other relation who has no children or whose children have already had an attack of measles.

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J. D. R.

VARICELLA

According to Stoeltzner, director of the University Paediatric Clinique at Halle, varicella of recent years has been characterized by an increasing severity which is shown by a more profuse eruption, a resemblance of the lesions to those of small-pox or vaccination, and greater disturbance of the general condition. The commonly accepted doctrine that varicella hardly ever leaves scars is no longer correct, scars now being frequently seen although the lesions had not been scratched. In one case the prodromal fever was so pronounced that small-pox would have been suspected, had not the child been recently successfully vaccinated. Stoeltzner reports another case complicated by staphylococcal pyaemia with multiple subcutaneous and intramuscular abscesses, and two others in which a relatively mild tuberculosis was unfavourably affected by the supervention of varicella.

Knoepfelmacher reviews the literature of accidental rashes in varicella, which, as was shown by Rolleston in 1907, may be prodromal, concomitant with the specific eruption or post-eruptive. According to the appearance of the lesions four varieties are described, namely, scarlatiniform, morbilliform, purpuric, and mixed. The distribution of the scarlatiniform rash, which is by far the most frequent, is not so typical as in scarlet fever, and mainly affects the trunk. The changes in the mucous membrane of the throat and tongue characteristic of scarlet fever are absent. The morbilliform rash, of which Knoepfelmacher reports a personal case, is relatively uncommon. The purpuric rash is very rare and of irregular distribution. The frequency of the various rashes in 48 cases collected by Cerf was as follows: scarlatiniform 41 cases, morbilliform 3 cases, purpuric 3, polymorphous 2. The pathogenesis of accidental rashes is still unknown, but they are probably due to the toxins circulating in the blood producing a form of vasomotor paralysis.

Paton records a case complicated by neuroretinitis in a boy aged 14. The attack of chicken-pox was very severe and there was some headache. On the third day of the illness it was found that the left eye was blind and the sight had remained defective ever since. On examination four months after the attack the left optic disk was pale, while the right was normal. There was a trace of albumin in the urine, but no evidence of organic renal disease.

von Bokay of Buda-Pesth records five cases in support of the view expressed by him in 1909 that the hitherto unknown virus of varicella may, under certain circumstances, appear in the form of herpes zoster. A total of nine similar cases had been published by him in 1892 and 1902. In each case the first disease was herpes zoster, which was followed after an interval of about two weeks, corresponding to the incubation period of chicken-pox, by the eruption of typical varicella in another individual. von Bokay suggests that some of the cases described by dermatologists as zoster generalisatus are aetiologically connected with these cases of varicella.

Meyer, of the Clinique for Infectious Diseases of the Düsseldorf Academy of Practical Medicine, inoculated 38 children with the contents of chicken-pox vesicles by scarification. 13 showed a local reaction in the form of papules and vesicles, and 25 had no local reaction. 5 of the former subsequently developed typical varicella towards the end of the third week after inoculation, though in each case of an extremely mild character. Of the 25 who were inoculated without any local reaction, 12 or 48 per cent. developed generalized varicella sooner or later after inoculation, but all after expiration of the incubation period for the natural infection. Of 39 children who were not inoculated 19 or 48·7 per cent. developed varicella, but the character of the attack was much milder in the inoculated than in the non-inoculated. Meyer concludes that inoculation against varicella is not a reliable preventive measure in all cases, but that it appears to guarantee a mild attack whether there is a local reaction or not.

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J. D. R.

INJECTIONS OF LIQUID PARAFFIN CAUSING CHRONIC INFLAMMATION—CHRONIC PARAFFINITIS

If the termination *-oma* is reserved for new growths, then it will best accord with what follows if the termination indicating an inflammation is employed, *paraffinitis* rather than the words *paraffinoma, vaselinoma, oleoma.* It is important to use the word paraffin in all medical references because it is the name of a material which does not undergo saponification; hence there is an objection to any term implying a resemblance to animal and vegetable oils, spermaceti, olive oil, &c., which undergo saponification and absorption in the body. The injection of paraffin having a melting-point such that at blood-heat it forms a soft solid was tried to remedy a sunken bridge of the nose, to prevent the prolapse of the rectum, to fill out a flaccid breast, to imitate a lost testicle. After a time the injected paraffin was found to start an inflammatory induration and to spread from the site of injection; the attempts to excise the mass proved most unsatisfactory.

Especially in France, liquid paraffin has been used as the medium for injecting camphor into the subcutaneous and subaponeurotic muscular tissues. In this country, liquid paraffin has formed a component of the bismuth and iodoform paraffin paste, commonly referred to as B. I. P. P. Although it has not caused such trouble as the subcutaneous and subaponeurotic injections of liquid paraffin, yet sinuses recur in stumps and bones in which the B. I. P. P. is found, on exploration, unabsorbed.

Jacob and Fauré-Fremiet, in 1917, gave a long account, including six cases, to illustrate the results of injections of liquid paraffin containing camphor. The practice appears to be continued in France, for Alglave has quite recently returned to the subject.

The subcutaneous and subaponeurotic injection of liquid paraffin causes no disturbance for a long while. Patients being ill at the time that the camphorated paraffin was injected have been unable to furnish a history of the injection. The disturbances commence after five months or two years or more from the injection, and are marked by indurations of a resistant, lobulated, or nodular character, which cause increasing pain and intermittent attacks of severe pain when nerves are involved. The induration spreads at its circumference to form a flattened mass, isolated nodules spring up in the course of the blood-vessels and the corresponding lymphatic glands become enlarged and hard. Meanwhile the skin is not involved and there is no increase of surface temperature or general disturbance. The induration is composed of dense fibrous tissue, honeycombed with small spaces and cysts in which the liquid paraffin is found. Drops of paraffin are widely distributed in the fibrous tissue, also englobed in large macrophages, which seem to be the means of conveying the paraffin away, so that nodules and indurations arise at some distance from the primary mass along the course of the lymphatics. The fibrous tissue is not vascular, for the blood-vessels show a thickening of the walls. The whole change is inflammatory and the presence of the paraffin can be distinguished by its failure to undergo saponification, which dissolves and removes animal fat.

Jacob and Fauré-Fremiet's cases were briefly as follows:

Case 1. A soldier, aged 34, received several injections of camphor in liquid paraffin in the course of a typhoid fever.

He returned to active service, but half a year later he began to notice indurations in the left thigh and left arm which disabled him. After a course of mineral-water treatment, then of arsenic, the pain continued to increase and kept him awake at night. There was found an induration which involved the aponeurosis and superficial fibres of the quadriceps extensor muscle; a second indurated mass adhered to the triceps in the left arm. In the right thigh there was a chain of hard nodules the size of peas along the line of the femoral vessels up to the groin, which were tender. Extensive excisions of the indurations were carried out one year and nine months after the injections, which left long puckered scars on the front of both thighs and in which a number of painful nodules re-formed. A month later, i. e. twenty-two months after the injections, fresh indurations appeared in the nape of the neck and midway between the occipital protuberance and the mastoid process. A further report two years and six months after the injections stated that the man continued to suffer from the painful indurations, which incapacitated him, and he was discharged from military service as unfit.

Case 2. A soldier after an antityphoid prophylactic injection suffered from fever and pains in the joints, for which camphor in liquid paraffin was injected into the thigh. One year and nine months later a painful nodule developed at the site of the injection, fixed to the aponeurosis and quadriceps muscle, from which a chain of nodules extended up to the groin, where the glands were swollen and hard. A wide excision was done, and after healing there reappeared a painful nodule, of the diameter of a franc piece, from which further trouble might be anticipated.

Case 3. A woman, aged 27, suffering from puerperal fever, had two injections of camphor in liquid paraffin into the deltoid muscle. Induration was noticed eighteen months later, and two years after the injection an indurated mass involving the deltoid and biceps was cut out, leaving a scar 15 cm. in length. There was subsequently a re-formation of painful nodules in the scar along with enlargement of axillary glands.

Case 4. A soldier, aged 24, supposed to be suffering from typhoid fever, had an injection of camphor in paraffin into the left arm. Two years later he begun to suffer from induration at the site of the injection, with loss of power in the arm. This induration, which measured 4 × 3·5 cm. in diameter, was cut out. Nodules re-formed in the scar and also fresh nodules appeared at the bend of the elbow. An inflammatory mass was removed by an extensive excision which included the dissecting out of the median nerve, which had become surrounded by dense fibrous tissue.

Case 5. A woman suffered from a broad induration in the thigh and from the recurrent nodules in the scar of the excision.

Case 6. A man in bad condition from pulmonary phthisis had several injections of camphor in paraffin into both his buttocks. The injections produced painful nodular indurations, widespread in both buttocks.

Case 7. A soldier, aged 32, who failed to afford a clear history was treated a long while as for syphilitic lesions. The cause of the induration was demonstrated by excising the masses.

Alglave's case had a remarkably long latent period. A woman, 16 years before, was suffering during her confinement from inflamed and painful breasts, for which she had many injections of 'camphorated oil'. Some nodes had persisted, but it was only after the above period that she noted that her breasts were enlarging and again becoming painful. The breasts presented multiple nodules, 12–15 in number, varying in size from a nut to half a mandarin orange; they were hard to the touch, irregular in contour, some were in the substance of the breast, some beneath the skin of the breast or over the sternum. The subcutaneous nodules were more or less adherent to the skin, which had become red in places as if an abscess were pointing. The left breast was removed, but the right breast and many other nodules were left. Bits cut out of the removed breast and dropped into water disclosed the paraffin, for it floated to the top.

Walther, in the discussion on Alglave's case, said that he had seen two women in whom paraffin had been injected into the breasts to remedy flaccidity. Both had obstinate fistulae from which small quantities of paraffin were discharged. The fistulae persisted after partial excisions and scrapings.

These French experiences show that the injection of liquid paraffin is just as objectionable as that of paraffin having a higher melting-point. It is not saponified in the tissues and is therefore not absorbed like animal and vegetable oils and glycerine.

Mook and Wander met with six cases in the United States, the first in 1913. 'Camphorated oil'—that is, camphor in liquid paraffin—had been injected repeatedly into the subcutaneous tissues and beneath the muscular aponeurosis of the arms and thigh. The description of the cases suggests that the injections were made into patients recovering from operations in a rather free and indiscriminate manner. In only one case were the indurations sufficiently localized to be excised; in the others, the masses were all deemed too extensive for excision, and the patients had to continue unrelieved. The applications of heat and massage increased the inflammation and favoured further spreading. Exposure to X-rays proved dangerous, for it disturbed the circulation and caused a tendency to necrosis and suppuration, which did not happen when the cases were left untreated. The authors refer to the indurations as 'tumours' and 'fibromas'. But the description of pieces removed for microscopical examination is the same as that noted above, dense fibrous tissue, not vascular, with spaces enclosing the paraffin.

Case 1. A woman, aged 31, after an operation for gall-stones, had injections of 'camphorated oil' every 15 minutes for several hours, altogether 2 or 3 dozen doses into the arms. These were painful for a short while and then nothing was noticed for 18 months, when indurations began to appear. She was first treated by arsenic internally, then by X-ray applications. After four years indurations extending to muscle were excised from both arms, each of the extent of the palm of the hand, with nodules running up to the axillae.

Case 2. A woman, aged 29, had had injections of 'camphor oil' into both arms and one thigh after an operation for double oophorectomy. The injections caused a temporary soreness. After four years small lumps appeared at the site of the injections which coalesced into indurated swellings, 2·5–10 cm. in circumference, which were slightly painful on pressure. 2½ years later there was no change from the conditions previously noted.

Case 3. A woman, aged 23, had 'camphor oil' injections after an operation for appendicitis. The lumps appeared one year later and continued to increase and become fused together. After five years there were deep-seated indurations in both arms and breasts, with chains of nodules up to the axillae, which were tender, and there were pricking pains after movements.

Case 4. A woman, aged 32, suffering in 1918 from pneumonia, had eight injections of 'camphor oil' into the right arm and three or four into the left arm. Lumps were first noted six months after the injections and then became increasingly painful.

Case 5. A woman, aged 45, had had, 1½ years before, both tubes and ovaries removed, after which 'camphor oil' was injected into the arms and thighs. Swellings were noticed four months after the injections, which continued to increase for three months.

Case 6. A woman was operated upon for gall-stones which was followed by pneumonia, and 'camphor oil' was injected on numerous occasions. 1½ years later lumps began to form in the arms and the induration increased to become 5 × 4 inches across.

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W. G. S.

ACUTE DILATATION OF THE STOMACH AND OF THE DUODENUM

A very grave condition results from high intestinal obstruction, of which there are three varieties: (1) Dilatation from obstruction below the junction of the duodenum and jejunum. (2) Dilatation of the stomach followed by that of the duodenum. (3) Dilatation of the duodenum from obstruction where the duodenum passes behind the mesentery and the superior mesenteric blood-vessels. The more frequent of the two latter is the primary dilatation of the stomach, but when the obstruction commences near the termination of the duodenum, which is compressed against the vertebral column by the mesenteric band, non-operative treatment fails. The washing out of the stomach and the prone posture which serve to relieve the gastric dilatation proves insufficient, and operative treatment done early in the case is the only remedy.

A dangerous or fatal dilatation of the stomach may occur in a healthy man, just as in animals. Sheep are always in danger of becoming 'blown', then dying within an hour; the rumen becomes rapidly distended by gas resulting from fermentation. Hungry animals rapidly eat green food wetted by dew or hoar frost, and with it they swallow air if feeding up wind; the careful shepherd interrupts the feeding for a while. Or the hungry sheep break out into the field of green wheat, which when eaten swells up in the rumen, and causes the condition called plenalvia. Relief is attempted by passing a hollow probang, or by puncturing the rumen through the epigastrium. The distension of the rumen induces kinking at both the cardiac and pyloric orifices, and rapid death is presumably due to compression of the heart and lungs through the diaphragm. Death has occurred in like manner when healthy men have gorged themselves with vegetable food. Finsterer included among his cases that of a soldier aged 40, who, following a meal of kohlrabi and turnip, was seized with pain in the abdomen, and vomiting. The epigastrium became greatly distended, there was no peristalsis, pulse 120. On passing a stomach-tube gas escaped with explosive violence, followed by 5½ litres of fluid. After the stomach had been washed out, the man was alternately placed on his right side and in the knee-elbow position. In a week the stomach was normal to X-ray examination. In Germany acute dilatation of the stomach is attributed to the administration of a general anaesthetic, especially ether, during which the patient swallows much air. Although it may be readily exaggerated, there is a certain degree of importance to be attached to the swallowing of air during the administration of an anaesthetic. There is also a variety of tic in which a neurotic patient swallows air, 'aerophagia'. Dilatation of the stomach is usually met with in patients suffering from some disease or injury. Beforehand there may have been no sign of gastro-duodenal disturbance, or the dilatation may supervene as an acute phase in a patient who has previously suffered from indigestion in a vague way.

In 1898, Box and Wallace described an acute and fatal dilatation of the stomach which had followed a blow on the epigastrium in a boy aged 16. Neither at the exploratory operation nor at the post-mortem examination was any obvious cause found for the dilatation. They added 'Abstracts of the fatal cases collected from Literature'. They conclude that the most probable explanation was a paralysis of the stomach wall and they advised as treatment gastric lavage, rectal feeding, and possibly the injection of strychnin.

In a further communication in 1901, Box and Wallace added two other fatal cases, one following a lacerated wound of the knee-joint and amputation, the other following pleuro-pneumonia. They considered that the first thing was a paralytic distension of the stomach which compressed the duodenum back against the spine.

Obstruction of the duodenum at the crossing of the mesentery was noted at a post-mortem examination in 1892 by Kelnyack in Manchester. A woman aged 19 had suffered from tuberculous disease of the hip and anaemia. She begun to vomit food, the vomit never became faecal; in spite of the washing out of the stomach, she died in 4 days. The stomach was found immensely distended, also the duodenum down to the point where it passed under the mesenteric blood-vessels. The jejunum and rest of the intestines were empty, and hanging, as it were, from the mesentery as a pedicle.

Haberer, in 1909 and again in 1917, contributed to the distinction of the two forms by which the duodenum may become compressed. The stomach in dilating presses downward the small intestines and so renders the mesentery taut, also it presses directly the duodenum from before backward against the vertebral column, and at the same time gives rise to kinking. The primary compression of the duodenum by the mesentery and blood-vessels occurs when the small intestines prolapse into the pelvis; this enteroptosis is predisposed to by wasting; it may follow upon the emptying of the abdominal cavity after distension by an ovarian cyst, uterine fibroma, or by pregnancy. There may occur a period during which the signs are of a chronic character. Then an acute phase sets in with signs of high intestinal obstruction; the pulse-rate is not lessened on emptying the stomach, as is in the case in primary gastric dilatation. There may be copious vomiting without any actual dilatation of the stomach itself. Indeed the stomach in chronic cases may show peristalsis and on exploration be found to have a thickened wall. The pylorus being patent, the vomiting is bilious, but undergoes no further change towards becoming faecal. Should there be delay, then the stomach is dilated secondary to the duodenum. As for the primary dilatation of the stomach, it is very important to relieve it at once; if it occurs after an operation, it should be recognized by the tympanitic distension of the epigastrium. The vomiting under such a condition should not be ascribed wholly to the anaesthetic. Following Schnitzler's proposal in 1895, Borchgrevink, of Christiania, in 1913 put forward the desirability of placing the patient in the prone position, in addition to washing out the stomach. This treatment may be expected to afford relief even when the duodenum is compressed owing to the small intestines having prolapsed into the pelvis, provided that they have not become fixed there by adhesions. The band which the mesentery then forms and which compresses the duodenum was noticed at post-mortem examination by Rokitansky. Treves, however, in his 'Intestinal Obstruction' appears to have deemed this prolapse of no importance.

Borchgrevink's statistics included 114 cases in which there was no treatment by position; 75 died, i.e. 63 per cent. 30 cases were treated prone, of whom 2 died, i.e. 7 per cent. 31 cases were treated 'medically', 29 died, i.e. 93 per cent. 29 were operated upon, and 21 died, viz. 72 per cent. Of these, in 6, the stomach was cut into and emptied, 5 died; in 7 a gastric fistula was made, 6 died; in 7 gastro-enterostomy was performed, 4 died; in 1 jejunostomy was done, followed by death; in 8, after an exploratory laparotomy, the stomach was emptied through the oesophagus, 5 died.

Doolin had his attention drawn to the subject by two cases. In one towards the end of an operation for the removal of a uterine myoma the stomach began to dilate, so a stomach-tube was passed and kept *in situ* until the tendency to dilatation was relieved. In a woman aged 19 who had suffered from puerperal fever, 'after a good dinner', there was acute epigastric pain and repeated vomiting. Two days later she appeared *in extremis.* The foot of the bed was raised upon a chair and the patient was laid prone whilst nutrient enemata containing brandy were given every three hours, together with subcutaneous saline infusion. Immediate relief followed and she left the hospital 20 days later. Doolin adopted the above treatment after reading Borchgrevink's paper. He proceeded to collect accounts of 188 cases, which he divided as follows:

(1) Unexpected sequelae to operations or post partum, 133 cases, i.e. 69 per cent. 96 were abdominal cases, the small intestines presumably sinking into the pelvis after the removal of an ovarian cyst, &c., or post partum.

(2) Unexpectedly supervening apart from operations, &c.: (*a*) Excessive eating and drinking; (*b*) spinal curvature; (*c*) acute and long-continued fever; (*d*) injury to the abdominal wall; (*e*) peritoneal inflammation; (*f*) occurring in apparent health.

At a number of post-mortem examinations it has been found that the mesentery compressed the duodenum in a way which could not be relieved by washing out the stomach and placing the patient prone.

Bäumler in 1901 described the case of a woman aged 25 admitted in the 2nd or beginning of the 3rd week of typhoid fever. After surviving complications, intestinal haemorrhage, and pneumonia, she had had for a fortnight a normal temperature, when she was suddenly seized with bilious vomiting; there was a tympanitic distension behind the umbilicus with a splash, but with occasional signs of gastric peristalsis; also motions were passed. Towards the last the stomach also dilated. She died 12 days after the commencement of the complications. The duodenum was dilated above the crossing of the mesentery, the pylorus was patent, and the stomach also dilated. The mesentery had compressed the duodenum back against the vertebrae and there was a bright red discoloration of the serous coat 2 cm. in breadth. Underneath this, in the mucosa, there was an almost complete ring of superficial necrosis, 1·5 cm. in breadth. Sections examined under the microscope after hardening showed that the compression had caused a disappearance of the villi and glands of the mucosa; the blood-vessels were dilated and some thrombosed. At the line of most constriction the mucous membrane had undergone necrosis down to the submucosa. The only other abnormalities were those connected with typhoid fever progressing towards healing.

Wortman's case presented several difficulties. A soldier was wounded by a shell; his right arm underwent a compound fracture in the upper third, and the brachial plexus was lacerated. After being simply dressed at the ambulance he was transported to the field lazaret. On the way he was seized with severe bilious vomiting and became collapsed. At the hospital he developed basal pleuro-pneumonia on the right side, resistance and tenderness in the epigastrium; the stomach was not then distended, whilst the hypogastrium was retracted; bilious vomiting persisted. For 10 days after the wounding the pleuro-pneumonia and the bilious vomiting continued, and then the epigastrium became distended owing to a dilatation of the stomach. The stomach was washed out repeatedly, after which the duodenum could be made out to be still distended and it yielded a splash. Elevation of the pelvis, the prone position, and even the turning on to the left side, could hardly be borne except for a short while, partly owing to the injury to the right arm and partly owing to the pleuro-pneumonia. The patient's condition not improving, 14 days after the wounding, an epigastric incision was made under local anaesthesia which exposed an enormous dilatation of the duodenum above the line of compression by the mesentery. This was taut owing to the small intestines having sunk into the pelvis. For fear of causing shock, the intestines were left undisturbed in the pelvis and a posterior gastro-enterostomy was done. The general condition improved so far that the epigastrium was retracted, flatus and motions followed enemas, and there was no more vomiting. But the pleuro-pneumonia increased and the gunshot wound became more septic, so that he died 24 days after being wounded. The post-mortem examination showed necrosis of the humerus and extensive broncho-pneumonia. The stomach was collapsed but the duodenum had remained enormously distended, because the small intestines had remained prolapsed, so keeping the mesentery tense. The gastro-jejunostomy had merely kept the stomach empty.

If the small intestines have become fixed by adhesions in the pelvis, neither the gastric lavage nor the prone posture can relieve.

In Wagner's case a woman aged 62 was attacked by peritonitis, and upon laparotomy under gas and anaesthesia this was found due to tubal suppuration on the right side with kinking causing gangrene of a coil of the ileum. The affected tube was removed; the gangrenous coil was excised, and an artificial anus set up. The patient did not improve and died a week later. The stomach was so dilated as to reach down to the iliac fossa; when this was raised the mesentery was seen to compress the duodenum owing to the small intestines being fixed by adhesions in the pelvis. But it appeared to be only a limited compression, for, after the stomach had been emptied and replaced in position, gas then passed backward through the pylorus from the dilated duodenum. The chronic partial obstruction of the duodenum by the tense mesentery had been rendered acute and complete by the kinking, following upon the secondary dilatation of the stomach.

Vogel described 4 cases of acute dilatation ending fatally in soldiers, in one of which the small intestines were fixed in the pelvis by adhesions.

Case I. A soldier aged 22, after being wounded in the thigh, had profuse suppuration. 3½ months later, and 9 days after the last surgical interference, he was seized with acute gastric dilatation and, in spite of repeated washings out of the stomach, died. The stomach was dilated and reached below the umbilicus, also the duodenum, being compressed by the mesentery of the small intestines which were mostly in the pelvis.

Case II. A soldier aged 25, with a compound comminuted fracture of the thigh, followed by suppuration, died 2 months later. 3 days before death bilious vomiting commenced, which was not improved by washing out the stomach and the prone position. A medium epigastrium incision was made, but, owing to the patient's state, nothing more was done, and he died the next day. At the post-mortem examination old adhesions consequent on appendicitis were found to have fixed the small intestines and to have caused the mesentery to form a tense band which compressed the duodenum.

Case III and *Case IV* were similar to *Case I.*

Two of Haberer's cases had the mesentery rendered taut by the drag of the small intestines; in one case the jejunum was contained in an irreducible and ventral hernia; in the other, the small intestines adhered to a uterus after ventrifixation. They were instances of primary duodenal compression, because the stomach was found empty and its wall hypertrophied.

Conclusions. The attention of the older observers was attracted unduly to the idea of a gastric paralysis, such as is set up experimentally by dividing both vagi nerves in an animal. This view should be discountenanced and replaced by a mechanical explanation.

Gastric dilatation is apt to arise unexpectedly and needs to be recognized at once; it should not be confused with post-anaesthetic vomiting; it should be distinguished from perforation, in a patient wasted by typhoid fever; it occurs as an indirect result of shock, including an abdominal injury which does not produce any obvious lesion.

Whenever the onset of dilatation of the stomach is but suspected, a stomach tube should be passed, the stomach washed out, the tube left *in situ* for a while, and the head kept low. Unless contra-indicated, the patient should lie on the face and the foot of the bed should be raised. If these measures are adopted early then the effects of the pressure and kinking due to the dilated stomach are avoided.

If there is not relief at once, as shown by the cessation of the bilious vomiting, together with a fall in the rate of the pulse, laparotomy must be adopted before the exhaustion of the patient renders operative interference too late. The chief measure to be carried out is raising of the small intestines from the pelvis, in order to release the mesentery, together with the separation of adhesions. Without this, gastro-jejunostomy is insufficient. Apparently gastro-jejunostomy is only indicated if there is pyloric obstruction of some form. It must be only exceptional that such operations as gastrotomy and evacuation of the contents, or gastrostomy combined with gastro-enterostomy and the passage of a tube through into the duodenum can be deemed necessary.

After the laparotomy and the relaxation of the compression of the duodenum, the patient's head should be kept low, with a stomach tube retained for a while, and even the prone position may be adopted.

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W. G. S.

PROPHYLAXIS OF PUERPERAL SEPTICAEMIA

The Registrar-General's Report for 1918 states that in England and Wales 2,509 deaths were assigned to pregnancy, representing 3·79 pro mille births, i. e. one woman died following pregnancy for every 263 children born. If 156 deaths from puerperal nephritis be deducted, then there were 3·55 deaths pro mille of births, or 1 in 281. Many surgical operations do not now put a woman in greater danger of losing her life. By due preparation before the commencement of labour and by care during labour puerperal fever is prevented from occurring in lying-in institutions, and outside these places, by adopting similar measures. But cases of abortion, premature and precipitate labour, do not lend themselves to such measures of prevention, and the pregnant women are busily engaged at home or at work, so that whatever they propose by way of preparation is likely to be put off to the last moment.

As soon as labour or abortion commences, a pregnant woman is in danger of infection from the micro-organisms on the skin of her external genitals, increased by the proximity to the anus. She is naturally protected against infection by way of the vagina, owing to the antiseptic properties of the vaginal secretion, which appears to be rendered more active by the setting in of pregnancy.

The epithelial lining of the uterus presents a barrier to invasion by organisms; in menstruation there is merely a desquamation; at the commencement of an abortion or labour, a breach is made in the epithelium, and a raw surface is exposed. There is formed a trail of blood from the uterine cavity down the vagina, which constitutes a line of ascent for the micro-organisms of the skin. Thus an inoculation of the raw surface exposed in the uterine cavity and the entrance of micro-organisms into the blood and lymph stream occurs independently of infection by indiscriminate digital examination, of douching, or of any lesion of the external genitals. In face of a primary puerperal septicaemia local measures are obviously of no avail. Septicaemia already started can only be controlled by the patient's power of resistance, assisted it may be by antitoxic sera or intravenous injections of antiseptics.

Against established puerperal septicaemia serum therapy or the intravenous injection of antiseptics has up to now generally proved useless. The same may be said concerning tetanus. Tetanus has been prevented by prophylactic injections, as soon as possible after the wounding. The corresponding opportunity for prophylaxis against puerperal septicaemia would be the administration of the serum or the intravenous injection of an antiseptic at the commencement, in every case, of abortion or of labour not previously prepared in a lying-in hospital.

With such a possibility in view, a pamphlet by Halban and Köhler is worthy of consideration. They give the history and post-mortem examination of 163 cases of puerperal septicaemia. Theirs should not be deemed a wearisome account of women doomed to death, or a mere repetition of what has been observed over and over again after death from puerperal septicaemia. Of particular value is the notification that in the great majority of the cases the micro-organisms, especially haemolytic streptococci, were identified in the blood during life.

The 163 cases died and were examined *post mortem* in the Gynaecological Section of the Wieden Hospital, Vienna, after their admission in various stages of puerperal septicaemia. The 73 coloured diagrams illustrate the multiple character of the lesions found. The post-mortem examinations were not only thorough from the general point of view, but they included a special examination of the genital organs and blood-vessels, as well as the blood-vessels of the lower extremities. The whole course of the pelvic vessels, also the renal veins and the inferior vena cava, were dissected out and slit open, in order to observe thrombosis, changes in the walls of the blood-vessels, as well as periphlebitis and periarteritis. The whole genito-urinary tract having been taken out and laid open, the uterus and annexa were examined by transverse, closely adjacent parallel incisions, by which lymphatic infection was distinguished from that by way of the blood-vessels. Then the blood-vessels of the lower extremities were exposed and cut open. The bacteriological examination of the blood was made repeatedly during life from a vein at the elbow. Cultivations from this blood were carried out under both aerobic and anaerobic conditions. Owing to the slow growth of streptococci full time was allowed for these organisms to develop in the cultures. An early opinion as to the haemolytic properties of the streptococci could be formed from the appearance of the fresh blood as it escaped from the vein. This was confirmed by the decoloration and decomposition of the blood in fluid media, also by cultivation on solid media. The primary importance of the repeated examination of the blood during life for the pathogenic micro-organisms is the essential feature of these observations.

After death, blood was taken from the right ventricle by burning through the wall of the heart, but this only served to confirm the observations made during life. The examination of discharges obtained from the vagina, cervix, and urethra proved of no value in deciding concerning the septicaemia.

The 163 were mostly mothers of families who had passed safely through previous pregnancies. Their ages averaged 31 years; 138 had been previously pregnant, on an average 3·3 times; thus only 25 were primiparas or gave no history of previous pregnancies. They had been engaged in hard work, or at any rate strain, and other abdominal injuries were frequently stated to have started the abortion or labour. The abortions, 93 in number, exceeded the number of labours, viz. 70; in one case only of abortion was there a lesion suggesting an artificial induction. Many of the women, before being admitted to the hospital, had been attended by doctors and midwives, but the general tendency of the case-histories is to suggest an infection independent of any inoculation in the course of digital examination, douching, manual removal of the placenta, or the curetting of placental remnants. There were of course ample opportunities for infection in this way; it is mentioned in one case that the midwife made 20 digital examinations. The cases became worse after curetting by the attending practitioners, but so also they did after the curetting in the hospital; in both instances the septicaemia had become established beyond the possibility of being arrested by any surgical measures. Moreover, there were patients who died from acute septicaemia, without being digitally examined or curetted. Reckoning from the first discharge of blood heralding an abortion, and from the date of a labour, the duration of the septicaemia until the day of death averaged 18·5 days, precisely the same in the case of the 93 abortions as in the 70 labours.

There were of course wide variations; 63 acute cases terminated within 10 days, 70 within 30 days, 30 lasted over a month, a few cases dragging on for 6 weeks to two months.

The blood was examined during life in 103 of the cases; among the 60 cases not so examined were some of the worst, who died soon after admission.

In 17 cases no organisms could be found in the blood; some of them were cases of long standing, the acute cases were not otherwise distinguishable from the rest.

In 86 cases the micro-organisms found were:
in 81 streptococci (haemolytic 56, non-haemolytic 24, anaerobic 1);
in 3 *Staphylococcus pyogenes aureus*;
in 1 *Bacterium coli*;
in 1 bacilli (Stäbschen).

Halban and Köhler sought to establish the course pursued by the infection in its spread from the uterine cavity by dividing the cases into groups according to the more prominent lesions found at the post-mortem examination as follows:

A. **Haematogenous.**

A (1). The blood-vessels chiefly involved without the formation of metastases; the lymph channels and fallopian tubes unaltered to the naked eye. 8 cases: 7 labours, 1 abortion; average age, 33·37. 7 cases previously pregnant, on an average 4·7 times. Duration of the septicaemia averaged 25 days.

Pathological lesions. Enlargement of the spleen in 8, degeneration of the heart muscles in 8; phlebitis and periphlebitis in 8, of the ovarian and uterine veins only in 2, along with the vena cava in 6; endometritis purulenta in 5 with placental remnants in 3, periproctitis in 1, cystitis in 2, parenchymatous nephritis in 2, pulmonary and pleural infection in 5.

Examination of the blood. Streptococci in 6, haemolytic in 4, non-haemolytic in 2; none found in 1 (A. 25 days' duration); not examined in 1 (L. with manual removal of placenta, 5 days' duration).

A (2). The blood-vessels chiefly involved, with metastases, the lymph channels and fallopian tubes not affected. 24 cases: 8 labours, 16 abortions; average age 32·5 years. 22 cases previously pregnant, on an average 4·6 times. Duration of the septicaemia averaged 27·7 days.

Pathological lesions. Enlargement of the spleen in 24, with infarcts in 2, and abscess in 1; thrombophlebitis in 24, limited to the ovarian and uterine veins in 6; endometritis purulenta in 15, with placental remnants in 13; pelvic cellulitis in 2, metastases in the kidneys in 16, in the lungs and pleura in 21, in the heart and pericardium in 8; panophthalmitis in 2, encephalitis in 1, parotitis in 1, otitis in 1, arthritis in 2, suppuration in skin and muscle in 7.

Blood Examination. Streptococci in 17, haemolytic in 13, non-haemolytic in 3, anaerobic in 1; single cocci not in chains 1; *Staphylococcus aureus* in 1 (A. 3¾ months' duration); none found in 2 (A. 11 days, A. 18 days); not examined in 3 (L. 14 days, A. 8 days, A. 26 days).

B. **Lymphogenous.**

B (1). Extension by way of the lymphatics without peritonitis, the blood-vessels and the fallopian tubes not being affected. 24 cases: 10 labours, 14 abortions; average age 31·2 years. 23 cases previously pregnant, on an average 4·4 times. Duration of the septicaemia averaged 27·6 days.

Pathological lesions. Enlargement of the spleen in 24, with infarcts in 4; endometritis purulenta in 16, parametritis in 4, kidney and bladder infection in 18, lungs and pleura infected in 12, the heart and pericardium in 11; panophthalmitis in 1, phlegmonous pharyngitis in 1, meningitis and encephalitis in 4, cerebral haemorrhage in 1, sinus thrombosis in 1, haemorrhage and abscess of skin and muscle in 4, arthritis in 3, jaundice in 3.

Blood examination. Streptococci in 16, haemolytic in 13, non-haemolytic in 2, anaerobic in 1; none found in 3 (A. 21 days, L. 16 days, A. 21 days); not examined in 5 (L. 28 days, L. 3½ months, A. 9 days, A. 22 days, A. 4 days).

B (2). Extension by way of the lymphatics, with peritonitis, the blood-vessels and fallopian tubes not being affected. 24 cases: 15 labours, 9 abortions; average age 30·4 years. 19 cases previously pregnant, on an average 3·2 times. Duration of the septicaemia averaged 17·7 days.

Pathological lesions. Spleen enlarged in 24, with an infarction, and an abscess in 1; peritonitis in 24, generalized in 20, limited in 4; endometritis purulenta in 23 with placental remains in 4, abscess in the uterine wall in 1, ulceration of the cervix in 1, parametritis in 7, ovarian abscess in 5, cystitis in 1, nephritis in 7, liver abscess in 2; lungs and pleura involved in 8, the heart and pericardium in 3; herpes in 1, jaundice in 1, encephalitis in 1.

Blood examination. Streptococci in 9, haemolytic in 4, non-haemolytic in 2; none found in 1 (L. 12 days); not examined in 14 (L. 11 days, L. 6 days, A. 7 days, A. 9 days, L. 12 days, L. 9 days, L. 12 days, L. 9 days, L. 2 months, L. 17 days, L. 7 days, A. 11 days, L. 8 days, A. 2 months).

C. **Salpingitis with peritonitis.** There were none of salpingitis without peritonitis among these fatal cases; the blood-vessels and lymphatics were not involved. 12 cases: 2 labours, 10 abortions; average age 30 years. 8 cases previously pregnant, on an average 5 times. Duration of septicaemia averaged 13·6 days.

Pathological lesions. Enlargement of the spleen in 12, salpingitis in 12 (10 bilateral, 1 left, 1 right), peritonitis in 12 (general in 10, limited in 2), endometritis purulenta in 8 with placental remnants in 5, bilateral ovarian suppuration in 1; kidney and bladder infection in 4, lungs and pleura involved in 2, the heart muscle in 12; parotitis in 1, jaundice in 1.

Blood examination. Streptococci in 4, haemolytic in 1, non-haemolytic in 3; not found in 1 (L. 9 days); not examined in 7 (L. 7 days, A. 4 days, A. 13 days, A. 5 days), but micro-organism in the peritoneal pus in 3, streptococci and *Bacillus coli* in 2 (A. 4 days, L. 36 days), cocci and Gram-negative rods in 1 (A. 11 days).

D. Combined Infections.

A and B (1). Combined haematogenous and lymphogenous infections without peritonitis, the tubes and peritoneum not being involved. 26 cases: 10 labours, 16 abortions; average age 32. 22 cases previously pregnant, on an average 5·5 times. Duration of septicaemia averaged 22·5 days.

Pathological lesions. Enlargement of spleen in 26, with anaemic infarct in 1; thrombophlebitis in 26, several vessels infected in 15, restricted in 11, to the left ovarian vein in 7 and to the right ovarian in 1, to the parametric veins in 2 and to the vena cava in 1. Heart and pericardium infected in 26, with definite lesions in 8, viz. of the valves in 3, mitral in 2, tricuspid in 1, suppurative pericarditis in 3, abscess in wall in 1, haemorrhages in 1; muscular degeneration in 18; lungs infected in 22, suppuration in 15, pneumonia in 7. Pleural empyema in 10. Endometritis purulenta in 19, with placental remnants in 5, and abscess in wall in 4; parametritis in 18, bilateral in 5, left in 9, right in 4; ovarian abscess in 3, left in 2, right in 1; cystitis in 2, dilated ureters in 1, pyelitis in 1; nephritis in 6, with abscess in 3; arthritis in 2, shoulder in 1, shoulder and ankle in 1.

Blood examination. Streptococci in 13, haemolytic in 5, non-haemolytic in 6, *Staphylococcus aureus* highly haemolytic in 1; not examined in 12 (L. 15 days, A. 21 days, A. 6 weeks, A. 7 days, A. 13 days, L. 6 days, L. 2½ months, L. 23 days, A. 31 days, L. 8 days, L. 35 days, L. 8 days).

A and B (2). Combined haematogenous and lymphogenous infection with peritonitis, the tubes not being involved. 9 cases: labour 3, abortion 6; average age 33·7. 8 cases previously pregnant, on an average 5·1 times. Duration of septicaemia 9·2 days.

Pathological lesions. Enlargement of spleen in 9; endometritis purulenta in 9 with placental remnant in 1, abscess of wall in 1, gangrene in 1; thrombophlebitis in 9; diffuse peritonitis in 9; ovarian suppuration in 3, right 2, left 1; ovarian infarct 1; parametritis in 5, bilateral in 2, right in 2, left in 1; kidney and bladder infected in 4; liver abscess in 1; lung and pleural infection in 5, heart and pericardium in 1.

Blood examination. Streptococci in 4, haemolytic in 2, non-haemolytic in 2; none found in 1 (A. 17 days); not examined in 4 (A. 10 days, L. 9 days, A. 4 days, L. 9 days).

A and C (1). Combined haematogenous infection with salpingitis without peritonitis. 1 case: abortion; aged 32, previously pregnant 4 times. Duration of septicaemia 16 days.

Pathological lesions. Spleen enlarged; bilateral salpingitis with a right ovarian abscess; suppurative thrombophlebitis extending into vena cava; multiple pulmonary abscesses.

Blood examination. Streptococci, slightly haemolytic.

A and C (2). Haematogenous infection with salpingitis and peritonitis. 3 cases: labour 1, abortion 2; average age 33·6. 3 cases previously pregnant, on an average 6 times. Duration of septicaemia before death, 20·3 days.

Pathological lesions. Spleen enlarged in 3; endometritis purulenta in 3; salpingitis in 3, bilateral in 2, left in 1; diffuse peritonitis in 3; thrombophlebitis in 3, parametric in 1, bilateral ovarian in 1, left ovarian in 1; pulmonary infection in 1.

Blood examination. Streptococci, haemolytic in 1, none found in blood in 1, but streptococci and *Bacillus coli* in the peritoneal pus (A. 6 days); not examined in 1 (L. 28 days).

B and C (1). Lymphogenous infection with salpingitis but without peritonitis. 8 cases: abortion 8; average age 29·75 years. 8 cases previously pregnant, on an average 3·75 times. Duration of septicaemia averaged 14·8 days.

Pathological lesions. Spleen enlarged in 8; salpingitis in 8, bilateral in 4, right in 2, left in 2, the peritoneal orifices were not closed, yet there was no obvious peritonitis; endometritis purulenta in 7, with placental remnants in 3; parametritis in 4, kidney and bladder infection in 3, heart and pericardium involved in 4, lungs and pleura infection in 5, encephalitis and meningitis in 3, cerebellar abscess in 1, panophthalmitis in 1.

Blood examination. Streptococci, haemolytic in 4, none found in 4 (A. 21 days, A. 21 days, A. 5 days, A. 4 days).

B and C (2). Lymphogenous infection with salpingitis and peritonitis. 13 cases: labour 2, abortion 11; average age 26·1. 8 cases previously pregnant, on an average 4 times. Duration of septicaemia averaged 20·3 days.

Pathological lesions. Spleen enlarged in 13; salpingitis in 13, bilateral in 4, right in 2, left in 7; endometritis in 12, with placental remnants in 4; peritonitis in 13, diffuse in 11, limited in 2; parametritis in 6, bilateral in 4, left in 2; ovarian abscess in 5, bilateral in 1, right in 1, left in 3; kidney and bladder infection in 8, lung and pleural infection in 4, heart and pericardium infected in 2, arthritis in 1, parotitis in 1.

Blood examination. Streptococci in 6, haemolytic in 3, *Bacillus coli* in 1, none found in 1 (A. 2½ months), not examined in 5 (A. 14 days, A. 16 days, L. 17 days, A. 7 days, A. 3 days).

A, B, and C (1). Haematogenous and lymphogenous infections combined with salpingitis, but without peritonitis. 3 cases: abortion 3; average age 30·6 years. 3 cases previously pregnant, on an average 3·6 times. Duration of septicaemia averaged 12·3 days.

Pathological lesions. Spleen enlarged in 3; thrombophlebitis in 3; endometritis purulenta in 3, with placental remnant in 1; salpingitis in 3, bilateral in 1, left in 2; parametritis in 3, right in 2, left in 1; ovarian abscess in 2, bilateral in 1, left in 1; lungs and pleura infected in 3.

Blood examination. Streptococci, haemolytic in 1, staphylococci in 1, none found in 1 (A. 14 days).

A, B, and C (2). Haematogenous and lymphogenous infection with salpingitis and peritonitis. 8 cases: labour 1, abortion 7; average age 29·3. 6 cases previously pregnant, on an average 3·3 times. Duration of septicaemia averaged 10 days.

Pathological lesions. Spleen enlarged in 8; thrombophlebitis in 8; salpingitis in 8, bilateral in 6, right in 2; peritonitis in 8; endometritis in 7, with placental remnants in 1; parametritis in 6, bilateral in 1, right in 4, left in 1; ovarian abscess in 4, right in 3, left in 1; kidney and bladder infection in 4; lungs and pleura infected in 8.

Blood examination. Streptococci in 3, haemolytic in 1, none found in 1 (A. 13 days), not examined in 4 (L. 10 weeks, A. 11 days, A. 8 days, A. 5 days).

The most important post-mortem observation was that the spleen was found enlarged in every case. It was the constant clinical evidence of the septicaemia, as much in the cases in which micro-organisms were not identified in the blood during life as in the cases in which they were found.

The fatal septicaemia was chiefly the result of streptococcal infection, for streptococci were also the micro-organisms found in such metastatic infections as the brain, meninges, eye, &c. It is evident that there was no opportunity for effective surgical treatment, and when the cases were admitted to the hospital it was too late for serum therapy or the intravenous injection of antiseptics.

Where there is no due preparation before labour or abortion, the case runs a risk like those exposed to infection by tetanus or typhoid fever, which can now be controlled by a prophylactic serum therapy.

Halban, J., u. **Köhler, R.** Die pathologische Anatomie des Puerperalprozesses und ihre Beziehungen zur Klinik und Therapie (mit 73 farbigen Textabbildungen). *Wien und Leipzig*, W. Braumüller, 1919.

W. G. S.

ANEURYSMS OF THE ABDOMINAL ARTERIES FOLLOWING GUNSHOT INJURIES

Aneurysms in the abdomen have been rarely caused by injury alone. Until the introduction of the modern rifle bullet most wounds of the abdominal arteries by gunshot ended quickly by haemorrhage. Griebel, in a long paper, collected references to abdominal aneurysms appearing after injury, but most of the early cases may be classed as essentially due to syphilis, the injury causing a rapid increase in the gravity of the aneurysm. He also, however, included records of some recent cases which occurred among the German wounded during the war.

Abdominal aorta. *Heyrovsky's Case*, 1915. The bullet entered over the region of the spleen and made exit on the right side near the liver, after passing transversely across the back of the abdomen. The wound was infected and a subphrenic abscess formed on the left side. 5 weeks later death occurred suddenly from intraperitoneal haemorrhage due to a false aneurysm of the abdominal artery having formed and ruptured.

Ribbert's Case, 1915. The bullet had passed through the body of a lumbar vertebra and after smaller haemorrhages death occurred from acute anaemia, 14 days after the injury. A splinter of bone from the vertebra had wounded the abdominal aorta, and an aneurysm the size of the fist had formed, lined by laminated clot, in places 1 cm. thick.

Common iliac artery. *Lengnick and Weiss's Case*, 1915. The bullet entered over the left hip and made exit two fingers' breadth above the fork of the groin. A swelling formed in the hypogastrium most prominently a little above the wound of exit; the swelling reached two fingers' breadth above the umbilicus, to the left as far as the ilium, and to a less extent to the right of the middle line. Dullness and pulsation were most marked over the lower part, a thrill was felt over the middle of Poupart's ligament, and a systolic bruit could be heard. An incision was made in the line of the iliac artery, starting from the middle line above the umbilicus. After clamping the abdominal aorta, the aneurysmal sac was cleared of clot and a hole found in the common iliac artery the size of a penny. This was cut out and the ends of the artery closed by sutures. After removing the clamp a pulse appeared in the femoral artery. A plug was placed in the aneurysmal sac and the wound sutured. The wound became septic, a duodenal ulcer formed and perforated, causing death, but there was no complication in respect to the aneurysm.

Orth's Case, 1915. The bullet entered the right side of the pelvis, the leg was held flexed by spasm of the iliopsoas muscle and there was great pain on attempting movement. A swelling formed above Poupart's ligament which did not pulsate; but in Scarpa's triangle a swelling the size of an apple appeared which pulsated. Eighteen days after the injury, an extraperitoneal incision was made, and, the aorta having been controlled by Momburg's method, the aneurysmal sac was opened and ligatures applied to both the common iliac artery and vein above and below the wound made by the bullet. Recovery was disturbed by cramping pains in the muscles and in the nerves, especially in the sole of the foot. Healing was complete in 6 weeks. But at the time of the operation slight disease of the pulmonary apices was noted and the man died 4 months later of phthisis.

v. Haberer's Case, 1916. The bullet entered at the outer border of the right rectus at the level of the umbilicus and made exit 7 cm. to the left of the sacrum. There followed pain along the track of the bullet and in the thighs. The legs were often oedematous, the motions irregular. Over the abdomen and in the lumbar regions a systolic bruit and continuous whirr could be heard, and just internal to the point of entry a pulsating swelling could be felt. On deep pressure the pulse in the right femoral artery disappeared. 14½ months after the injury an arterio-venous aneurysm, the size of an egg, which had formed between the right common iliac artery and the inferior vena cava, was exposed. This was treated by separating the two vessels and closing the opening in each, the size of a large bean, by means of sutures. After this no pulsation could be felt in the arteries below, but healing, nevertheless, occurred without complications.

Internal iliac artery. *Gobiet's Case*, 1917. A shrapnel ball entered the thigh and lodged in the pelvis; severe haemorrhage followed from the bowel, and per rectum a large tense pulsating tumour was felt to the right side of the pelvis, which communicated with the lumen of the rectum through a small opening. 16 days after the wounding, the right internal iliac was exposed across the peritoneal cavity and the artery tied before its entry into the aneurysm. Then an incision was made beside the rectum from below and the contents of the sac, which had become foul, evacuated. Healing followed.

Fromme's Case, 1917. A volunteer officer was wounded in several places, and amongst the rest by a bullet which entered the pelvis. This caused difficult micturition and paralysis of the left peroneal muscles. Six weeks later there was a swelling in the hypogastrium the size of two fists, which was tender on pressure and dull to percussion. Emptying the bladder made no change in the swelling. 2½ months after the injury, through an opening as for excision of a cancer of the rectum, a retroperitoneal aneurysm, the size of a child's head, was exposed, a branch of the internal iliac tied in two places, and the contents of the aneurysm evacuated. Healing followed. The peroneal paralysis persisted.

Renal artery. *Kaunitz's Case*, 1916. A man died 59 days after being shot in the abdomen. P.M. it was found that the bullet had passed through the stomach and had set up an abscess between the stomach and spleen, pancreas and transverse colon, into which the abscess had opened. The upper two-thirds of the left kidney had shrunk following infarction. The renal artery presented a dilatation the size of a small hazel nut filled with clot which had blocked the branches distributed to the upper two-thirds of the kidney. Death had been due to septic pericarditis and pyo-pneumothorax.

Hepatic artery. *Käding's Case*, 1919. A rifle bullet had passed through the right half of the liver into the pleura, causing an extensive haemothorax, which was treated by incision and drainage. 11 weeks later attacks of cramping pain in the hepatic region occurred, blood-clot was vomited and tarry stools passed, without jaundice. About 4 months after the injury the liver was exposed on the diagnosis of a subphrenic abscess, but only dilatation of the hepatic artery with a whirr was made out. The tensely distended gall-bladder was stitched to the skin and opened some days later, when blood-clot escaped. Hence an aneurysm of the hepatic artery was diagnosed. Blood continued to be discharged from the gall-bladder, also by the intestines, so, 17 days after the cholecystotomy, the hepatic artery was exposed above the middle of the lesser curvature of the stomach and ligatured. The aneurysm could not then be felt and was therefore supposed to be within the substance of the liver. Healing occurred in 2 months. 3½ years later the patient was in remarkably good health.

Superior mesenteric artery. *Böttner's Case*, 1919. A wound in the abdomen by a fragment of shell set up a severe gastric pain which continued until one day there occurred, without obvious cause, signs of internal haemorrhage. The patient was operated upon at once and intraperitoneal haemorrhage from an aneurysm exposed, but he died on the table. *Post mortem* it was found that an aneurysm of the superior mesenteric artery had formed around the shell fragment and had become partly filled with clot. Its wall had then given way.

Splenic artery. *Grosser's Case*, 1916. There was an infected gunshot wound of entry and exit involving the last 3 ribs on the left side. Repeated haemorrhage from the wound of exit occurred in spite of plugging. The general condition of the patient contra-indicated active treatment, and 9 weeks after the injury he died following upon a further severe haemorrhage. Between the diaphragm and the spleen there was found a cavity the size of the fist and from the surface of the spleen forming part of the wall of the cavity projected an aneurysm the size of a walnut, which had leaked.

Griebel's Case, 1915. A rifle bullet entered to the left of the spine of the 4th lumbar vertebra, passed through the lower pole of the kidney, divided the splenic artery at the hilum, and traversed the diaphragm and the lower lobe of the lung. The wound of exit was two fingers' breadth under the left nipple. Whilst the rest of the track of the bullet healed without disturbance, an aneurysmal sac developed at the hilum of the spleen. About 5 weeks after the wounding, the man, after having been apparently convalescent, begun to complain of pain in the stomach, and some days later there was a sharp attack of intraperitoneal haemorrhage. From this the patient recovered slowly until 16 days later, when he had a second attack, which was supposed to be due to suppuration in the blood-clot previously extravasated. An incision exposed old and recent clot, but the bleeding-point could not be found, hence the spleen was excised. The patient died before the wound could be sutured. At the post-mortem there were evidences of blood entravasation all over the abdominal cavity. The aneurysmal sac had been formed by peritoneal adhesions around the divided splenic artery and was the size of the fist.

Griebel, E. Ueber traumatische Bauchaneurysmen im Anschluss an einen Fall von falschem Aneurysma nach Abschuss der Milzgefässe, und einen Fall von traumatischem intrahepatischem Aneurysma. *Deutsche Ztschr. f. Chir.*, 1920, **155**, 312.

W. G. S.

THE PATHWAYS OF THE CEREBROSPINAL FLUID

Although since the introduction of lumbar puncture in 1891 investigations into the pathological changes in the cerebrospinal fluid have been extensively and profitably carried out, and forms of treatment which utilize this fluid as a vehicle for the conveyance of drugs and other substances to the central nervous system have been widely employed, yet our knowledge of the pathways of the cerebrospinal fluid and of its physiological relationships to the nervous system and to the other body fluids, the blood and lymph, is still very incomplete. However, while this ignorance renders intraspinal therapy largely empirical, it seems in no way to have embarrassed the advocates of this form of treatment.

Many obscure aspects of the problem have been rendered clearer by the series of studies on the cerebrospinal fluid and its pathways made by Cushing and his co-workers at Harvard (1914–15), and the subject of the present short review.

In a preliminary paper, Cushing formulates some of the problems to be solved. Assuming that the choroid plexuses are the chief source of the cerebrospinal fluid—and this, Cushing states, has not been conclusively proved—is the process one of secretion, filtration, or of dialysation? What conditions activate and what inhibit these choroidal glands? Have they an internal as well as an external secretion? To what primary diseases are they subject? How early in embryonal life do they secrete? Why does the fluid they secrete differ so widely from that secreted by most other glands? Why are its cells so impermeable to the passage from the bloodstream of drugs and of substances such as bile pigment, which in jaundice quickly stain all the other body tissues and fluids? Does the secretion receive accessions from the pineal or pituitary glands or from the ependyma? Are there lymph channels in the brain, and, if not, how does the central nervous system dispose of its products of tissue waste? If there are cerebral lymphatics, do they discharge into the subarachnoid space, and, if so, is the ventricular fluid the same chemically, physically, and cytologically as that in the subarachnoid space?

So much for the questions arising from a consideration of the source and nature of the fluid; its pathways of escape have still to be discussed. This question is dealt with in detail and very conclusively by Weed in the second and third papers of the series.

(1). **The pathways of escape from the subarachnoid spaces.** The cerebrospinal fluid is poured out into the cerebral ventricles, whence it escapes from the fourth ventricle by the foramina of Magendie and Luschka into the cranial subarachnoid space. It is then free to pass forward over the hemispheres or caudally into the spinal subarachnoid space. The cranial and spinal subarachnoid spaces correspond, but while in the spinal theca dura and arachnoid are in close opposition, in the skull the arachnoid and the pia adhere closely to form the pia-arachnoid. The cerebrospinal fluid does not pass into the subdural space, and normally the subdural fluid in the skull forms a capillary layer. On its inner and outer surfaces the arachnoid membrane is covered by a layer of mesothelial cells and the subarachnoid spaces are similarly lined throughout.

Key and Retzius, whose work on this subject was published as long ago as 1876, regarded the Pacchionian granulations as the sole channels by which the cerebrospinal fluid left the subarachnoid spaces and regained the circulation in the cerebral sinuses. They injected the subarachnoid spaces with a solution of coloured gelatin and traced the resulting injection mass into the cerebral sinuses through these granulations. This view was accepted until it was realized that these structures are absent in animals other than anthropoids and man, and are only present in these in adult life.

Weed gives a comprehensive summary of the various views that have been advanced since the time of Key and Retzius, and concludes that although the general opinion is that other channels of absorption must exist, yet no anatomical proof of their existence has been furnished.

Experimental methods. Of the various possible methods of determining the channels of escape, the one finally adopted by Weed is based upon the prussian-blue reaction. An isotonic solution containing equal parts of potassium ferrocyanide and iron ammonium citrate is injected into the spinal subarachnoid space of an anaesthetized animal (cat, dog, or monkey). The brain and its envelopes are then removed and fixed in a formalin solution containing 1 per cent. HCl. The resulting precipitate of ferric ferrocyanide (prussian blue) consists of a fine granular deposit. There is no general tissue absorption of the injection solution, and the course which it follows may be taken as the true pathway of absorption of the normal cerebrospinal fluid. Using this method, Weed found prussian blue granules clinging closely to the meshes of the subarachnoid spaces, but never in the subdural space, the lining mesothelium of the subarachnoid space being impermeable to the injection solution.

The arachnoid villus. Weed was able to trace the fluid from the deposition of prussian blue granules into the Pacchionian granulations and also into more numerous and widely distributed structures which he names the arachnoid villi. These constitute the normal channel of drainage into the cerebral sinuses. They are most numerous about the vicinity of the various venous sinuses, particularly the superior longitudinal and the cavernous sinuses, but are found associated with all the smaller sinuses at the base of the skull. The villi are delicate web-like structures of many interlacing strands prolonged from the arachnoid to the walls of the dural sinuses. In the neighbourhood of the superior longitudinal sinus they commonly ensheath the large cortical veins as these pass from the sulci to the sinus.

As the villus nears the sinus its structure changes. Its connective tissue network becomes closer, and as it invades the fibrous dura it forms a delicate core of myxomatous tissue. Covering the core is a layer of mesothelial arachnoid cells, which maintain the continuity of the villus and constitute the cellular filter into the cerebral sinuses. The head of the villus lies in the substance of the dural wall of the sinus or projects into the lumen of this, and is capped by a tuft of mesothelial cells in several layers. The whole is covered where it lies in the sinus by the endothelial lining of this vessel. Large, warty, sessile, or pedunculated masses of arachnoid mesothelial cells are to be found in the dural walls of the sinuses. In anthropoids and man, villi are very numerous in the irregular diverticula (lacunae laterales) of the superior longitudinal sinus into which the cerebral veins open before discharging their contents into the sinus. The passage of fluid from these villous structures into the sinus is seen by the precipitation *in situ* of the injection fluid, and the precipitated granules may be traced from the subarachnoid spaces into the lumina of the sinuses. Cell nests of arachnoid mesothelial cells are widely scattered throughout the dura, especially in the neighbourhood of the sinuses. They are in continuity with villi and they probably serve as intradural channels for the passage of cerebrospinal fluid. Evidence of such a circulation of cerebrospinal fluid is obtained from the observation of bleeding from the outer surface of the dura when this is exposed by the removal of bone or the elevation of osteoplastic flaps. In these circumstances the blood oozing from the dura is very thin and watery, and also spots of clear watery exudation may be seen on the surface of the membrane.

Weed considers that the fluid escapes through the cells covering the villus by a process of filtration from a point of higher to one of lower pressure, and of osmosis from a fluid of low colloid and crystalloid content to one of higher. Probably there is very little drainage from the spinal subarachnoid space.

The Pacchionian granulations. Weed regards these as large hypertrophic villi which have become macroscopic in size. Cushing and Weed (Study IX), studying the formation of calcareous deposits in the arachnoid, find that this is commonly associated with a hyperplasia of the arachnoid mesothelium, and from their structure it seems that the so-called **dural endotheliomata,** which show the same cellular arrangements with calcareous and caseous deposition that occur in the arachnoid, arise from the arachnoid mesothelium.

An accessory or lymphatic pathway of absorption. In addition to the venous pathway described, there is evidence of an accessory pathway through the lymphatic system. Key and Retzius were able to inject the cervical lymphatics from the spinal subarachnoid space and later observers have obtained similar results. Weed found after his subarachnoid injections that the cervical lymphatic channels and glands and the perineural lymphatics of the cranial nerves in the neck were deeply stained by prussian blue. Evidently, the well-recognized extension of the subarachnoid space along the cranial nerves from their points of exit from the skull must be continuous with the perineural lymphatic channels, or at least capable of injection from these. It was found that the injection fluid passed along the olfactory nerves through the cribriform plate and into connective tissue spaces beneath the nasal mucosa, whence it passed into submucous lymphatic spaces. The cervical lymphatic channels were reached from these. In some instances a cerebrospinal rhinorrhoea occurred.

(2). **The dual source of the cerebrospinal fluid.** Weed undertook a further series of observations to ascertain the processes of elaboration of the cerebrospinal fluid. Though it is now accepted that the cerebrospinal fluid has a double origin—from the choroid plexuses and from the perivascular spaces—there is as yet no conclusive evidence for this belief. To obtain a result which would indicate only the fluid secretion of the choroid plexuses and exclude the fluid coming from the perivascular channels, Weed catheterized the third ventricle. The procedure entails considerable operative interference which need not be described here. In this way the action of drugs and other substances upon the activity of the choroid plexuses can be studied. (cf. Dandy's more recent observations. *Medical Science*, 1920, **1**, 511).

In the eighth paper of the series Cushing and Weed employed an improved method of tapping the ventricles by sagittal puncture through the superior longitudinal sinus. In this way they determined that intravenous injection of extract of posterior lobe of the hypophysis increased the flow of cerebrospinal fluid by direct stimulation of the secretory activity of the choroid plexuses.

The perivascular channels. These extend to the finer capillaries. The use of the terms 'lymphatics' or 'lymph spaces' as applied to these channels is, Weed holds, unsatisfactory, since it indicates a lymph content in them. It seems from Spina's observations that the normal direction of flow in these spaces is centrifugally into the subarachnoid space. Weed believes that in these spaces are carried away the waste products of nerve cell metabolism, which flow into the cerebrospinal fluid. Thus, the fluid obtained by lumbar puncture consists of the secretion of the choroid plexuses and also the dissolved waste products of the central nervous system coming from the perivascular spaces. There is reason to suppose that the fluid contents of these spaces is not lymph but a fluid of much simpler composition. Weed found that in injections made under moderate pressure, prussian blue granules passed from the subarachnoid spaces into the perivascular channels as far as the capillaries. There was also in some instances evidence of injection of the perineuronal spaces, indicating, as Mott has suggested, that the perivascular and perineuronal spaces communicate. There was no evidence of the passage of injection fluid into the vessels themselves from the perivascular spaces, and Weed thinks that in all probability fluid normally passes from the capillaries into the perivascular spaces containing nutritive substances, and then passes away into the subarachnoid space with waste products in solution. In conclusion, Weed states (p. 110) that 'this whole accessory fluid system of the cerebrospinal axis—an intramedullary canalicular system—undoubtedly possesses an active function in maintaining the metabolic exchange and elimination of the nerve-cells. Throughout the body in other tissues there is a chief and accessory circulation. For in these other tissues of the body there is in addition to the blood capillary a lymph capillary with the tissue juice or plasma playing the intermediate part in exchange. Nervous tissue lacks entirely the lymphatic system; it would appear that its place is taken by the perineuronal, pericapillary, and perivascular system with its contained fluid, and that this fluid is poured into the subarachnoid space, where it mixes with the fluid from the choroid plexuses'.

(3). **The drainage of intra-ocular fluids.** (Wegefarth.) In an introductory study (No. V.) Wegefarth gives an historical review of our knowledge of the intra-ocular fluids. His own experiments were carried out on the rabbit, cat, dog, and monkey, and consisted in the intra-ocular injection of a solution similar to that employed by Weed and already described. Fixation was then carried out in HCl formalin solution.

The main sources of the aqueous fluid of the eye are the ciliary body and processes, whence the fluid passes into the anterior chamber to the angle from which it passes into the blood-stream. Wegefarth finds that in the pectinate ligament are '*pectinate villi*' in structure and function like the arachnoid villi already described. The waste products of the retinal neurones pass by perineuronal spaces into the aqueous reservoir, and the drainage of intra-ocular fluid, which is thus seen to be of dual origin, is similar to that of the cerebrospinal fluid.

(4). In the seventh study of the series, Wegefarth and Weed compare **the processes of fluid drainage in the cerebral and ocular systems.** They draw attention to the resemblance between the meninges and the tunics of the eye (dura and sclera, pia-arachnoid and uveal tract), to the sources of the fluids in each case (choroid plexus and ciliary body), to the accessory sources of fluid in each case (perineuronal and perivascular), to the identical mode of absorption of the fluids, and finally to the physical and chemical resemblance of the fluids in each case. They have been able to demonstrate direct communication between the two fluid systems along the perivascular spaces about the central vessels.

They conclude that 'the functions of the fluids contained within the dura and within the sclera are in many ways quite similar. Both serve as fluid reservoirs in which are supported delicate structures which, deprived of this watery cushion, would soon be harmed. Both carry away the waste products of cellular activity; both maintain the proper distension of their organs. Apparently neither fluid has any relation to the nutrition of the surrounding tissues except in the non-vascular trabeculae and membranes. A direct communication between the fluid cavities and the venous sinuses is likewise possible in both organs. . . . There is almost complete anatomical and physiological correspondence between these fluid relations in eye and cranium; the secretion, the course of the fluid, the ultimate return to the major circulation—all of these are wholly similar processes.'

Cushing, H. Studies on the cerebrospinal fluid and its pathway. I. Introduction. *J. Med. Research,* 1914, **31**, 1.

Weed, L. H. (1). Studies on the cerebrospinal fluid and its pathway. II. The theories of drainage of cerebrospinal fluid, with an analysis of the methods of investigation. *J. Med. Research,* 1914, **31**, 21.

Weed, L. H. (2). Studies on the cerebrospinal fluid and its pathway. III. The pathways of escape from the subarachnoid spaces, with particular reference to the arachnoid villi. *J. Med. Research,* 1914, **31**, 51.

Weed, L. H. (3). Studies on the cerebrospinal fluid and its pathway. IV. The dual source of cerebrospinal fluid. *J. Med. Research,* 1914, **31**, 93.

Wegefarth, P. (1). Studies on the cerebrospinal fluid and its pathway. V. The drainage of intra-ocular fluids. *J. Med. Research,* 1914, **31**, 119.

Wegefarth, P. (2). Studies on the cerebrospinal fluid and its pathway. VI. The establishment of drainage of intra-ocular and intracranial fluids into the venous system. *J. Med. Research,* 1914, **31**, 149.

Wegefarth, P., and **Weed, L. H.** Studies on the cerebrospinal fluid and its pathway. VII. The analogous processes of the cerebral and ocular fluids. *J. Med. Research*, 1914, **31**, 167.

Cushing, H., and **Weed, L. H.** (1). Studies on the cerebrospinal fluid and its pathway. VIII. The effect of pituitary extract upon its secretion (choroidorrhœa). *Am. J. Physiol.*, 1915, **36**, 77.

Cushing, H., and **Weed, L. H.** (2). Studies on the cerebrospinal fluid and its pathway. IX. Calcareous and osseous deposits in the arachnoidea. *Johns Hopkins Hosp. Bull.*, 1915, **26**, 367.

F. M. R. W.

ABSTRACTS

SURGERY

Runeberg, B. Om de s.k. aseptiska renala pyurierna jämte några ord om hematogena infektiösa nefriter och pyelonefriter. [**The aetiology of the so-called aseptic renal pyuria; haematogenous infectious nephritis and pyelonephritis.**] *Finska läk-sällsk. handl.* 1920, **62**, 165–209.

In a surgical hospital in Helsingfors, Runeberg investigated all the cases of aseptic renal pyuria treated in the period 1900–18. Of the 56, in which there was no history of gonorrhoea, 30 were treated by operation, 26 by more conservative methods. In 11 out of the 30, the kidney showed at the time of operation definite macroscopic signs of tuberculosis. In 3 other cases the macroscopic evidence was negative, but a careful microscopic examination revealed tuberculosis. Of the 26 cases treated on conservative lines, 4 subsequently proved to be tuberculous. In other words, out of a total of 56 cases, barely a third proved beyond doubt to be tuberculous. Runeberg contrasts these findings with the teachings of Rovsing, Suter, and others, who regard as inevitable the diagnosis of tuberculosis even when repeated bacteriological examination of the urine is negative.

In further support of his view that many cases of aseptic renal pyuria are not tuberculous, Runeberg observes that all the 10 patients, on whom nephrectomy was performed without tuberculosis or renal calculus being found, were still alive and well. He compares these cases with 93 in which nephrectomy for definite tuberculosis was performed in the same period. The post-operative tuberculous mortality among these patients was over 20 per cent. Further, 20 patients whose aseptic renal pyuria was treated on conservative lines in the same period were still alive and well. No such claim could be made for the 87 patients whose urine contained tubercle bacilli, and who were also treated on conservative lines.

Runeberg defines with considerable clearness the features characteristic of non-tuberculous, sterile, renal pyuria. First he excludes the cases of calculus, 7 of which were associated with sterile pyuria. A striking feature of the remaining cases was the frequency with which the excised kidneys showed signs of congenital defectiveness. These morphological anomalies probably played a most important aetiological part. Another distinctive characteristic was the comparative frequency with which males were affected; of 30 cases only 7 were females. In other suppurating conditions of the kidneys the sex ratio is reversed. Although sterility of the urine was the first condition qualifying these cases for inclusion in this class, Runeberg regards this distinction as more or less misleading; for between the consistently sterile and septic forms of renal pyuria he observed a few cases in which the urine was alternately sterile and septic. In other cases, again, the urine was sterile, but sections of the kidney showed a few micro-organisms which were usually staphylococci. He devotes several pages to discussing the mode of infection, which he considers is primarily by the blood-stream. The sequence of events is: haematogenous infection giving rise to focal, glomerular nephritis, which in turn sets up pyelitis and 'elimination' foci in the medulla of the kidney. The pyelitis induces an ascending, lymph-born, interstitial nephritis ; and this progresses by thrombosis and embolism, giving rise to extensive, subcapsular, wedge-shaped foci.

Differential diagnosis and treatment. The differentiation between this condition and tuberculosis is difficult. Not to perform nephrectomy on a case of unilateral renal tuberculosis is a more serious error than to undertake this operation on the mistaken assumption that the condition is tuberculous. Even when tuberculosis can be excluded, nephrectomy may yet be advisable, and it is indicated when the pyuria is strictly unilateral, has lasted a long time, and has reduced the patient to complete or partial invalidism. The probability that the kidney is congenitally defective weighs in favour of nephrectomy. Runeberg confirms Colombino's observations as to the differences in the pus cells of tuberculous and non-tuberculous renal pyuria. Though the mononuclear and the polymorphonuclear pus cells occur in the same proportion in both conditions, the pus cells of tuberculosis are irregular and notched, staining badly and unevenly. They also show dissolution of protoplasm and of nuclei, as well as vacuole formation ; in non-tuberculous infections the pus cells are round and stain normally. Another valuable aid to diagnosis is the history and course of the case. The onset of the non-tuberculous pyuria is comparatively rapid, and the disease has usually culminated in a few weeks. Relapses or exacerbations are common to both diseases ; but their duration is shorter in non-tuberculous disease. The latter also responds quickly to rest in bed, urinary antiseptics, dieting, and flushing the system with water ; and it is characteristic of non-tuberculous disease that the symptoms rapidly return when this treatment is given up too soon. Runeberg has found the cystitis associated with this condition clear up as effectively after nephrectomy as a tuberculous cystitis clears up after removal of a tuberculous kidney. C. L.

Platou, E. Om akute empyemer og deres behandling. [**The treatment of acute empyema.**] *Norsk Mag. f. Lægevidensk.*, 1920, **81**, 666–96.

Platou's analysis of 105 cases of acute empyema with 18 deaths (17·1 per cent.) covers the influenza period of 1918–19 in Christiania. His cases were treated in two departments of the Riks-hospital, where different lines of treatment were adopted. In both departments ribs were resected, but in one the empyema was treated as a closed lesion, and drainage was effected by syphonage through a Pezzer's catheter No. 26–28 carefully sewed into the wound. In the other department, after pus and fibrin had been removed, a thick drainage tube, 5 to 10 cm. long, was inserted, and the dressings were changed once or twice a day. A comparison of these 'closed' and 'open' methods showed little difference in the mortality, but the average duration of treatment was 39 days for the 'closed' cases and 59 for the 'open'. P. finds the 'open' method entails secondary infection, and has little good to say for it. He also notes that influenzal empyema shows a greater mortality, debilitates the patient more, and requires longer treatment in hospital than ordinary empyema. Influenzal empyema develops earlier, and, as a rule, the effusion is greater than in the case of ordinary empyema. Operative treatment should not be undertaken till the acute stage of the lung disease has subsided. C. L.

Schmiegelow, E. Kliniske bemærkninger vedrörende cancer laryngis et pharyngis, særligt med hensyn til dens behandling. [**The treatment of cancer of the larynx and pharynx.**] *Hosp.-Tid.*, 1920, **63**, 385–91, 401–7.

Since Schmiegelow lectured in London in 1914 on the results of the treatment of intralaryngeal cancer with the help of laryngo-fissure, he has added 24 to his 66 cases, bringing the total up to 90 cases in which the disease was confined to the interior of the larynx. In 45 cases the primary disease was situated in the vocal cords, and these were probably the seat of the primary disease in many of the other 45 cases, several of which were so advanced when first examined that it was impossible to decide the position of the primary disease. Among many of the 33 patients, whose disease was advanced when first seen, definite hoarseness, pointing to primary involvement of the cords, had been the first symptom. In addition to this predilection of primary cancer for the cords, S. found endolaryngeal cancer to be far more common in males than females; of 25 patients with primary disease of the cords, 23 were men. The fate of the 90 patients is thus analysed:

	No.	Cured.	Dead or Relapsed.
No treatment	22	0	22
Tracheotomy	9	0	9
Intrinsic removal of cancer—			
Endolaryngeal	5	1	4
by laryngo-fissure, *alias* thyrotomy	39	22	17
by pharyngotomy	1	0	1
Partial resection of larynx	4	0	4
Total resection of larynx	10	1	9
Total	90	24	66

With regard to the cases of laryngo-fissure, 7 terminated fatally from pneumonia or haemorrhage in connexion with the operation. Of the 32 patients surviving the operation, 10 died of relapse and 22 were cured, but the observation period was too short to be decisive in the most recent cases. Of late years S. has abandoned the practice of a preliminary exploratory excision for fear of opening channels and promoting metastases, and he relies solely on the course of the disease, the history, the laryngoscopic picture, and the exclusion of syphilis and tuberculosis for his diagnosis. Hitherto he has not made a diagnostic mistake in the cases he has operated on for malignant disease. Before 1914 he always operated under general anaesthesia; since then he has operated under local infiltration anaesthesia with novocain and suprarenalin. After the wound has healed, in about eight days, and before the patient is discharged, he gives a preventive course of X-ray treatment with a view to neutralizing any malignant foci that may remain after the operation.

Although the prognosis for cases of primary disease of the cords operated on early was found to be good, it was comparatively bad when the endolaryngeal disease began elsewhere than on the vocal cords. The mortality among the 12 men and 5 women in this category was very high. S. concludes this chapter on cancer of the larynx with a reference to the promising possibilities of radium. He finds it a comparatively easy undertaking to keep a tube of radium steady in the larynx after tracheotomy has been performed and the tube of radium has been secured to the tracheotomy cannula.

Among the 19 cases of retrolaryngeal cancer of the pharynx treated during the last 5 years there were as many as 15 women. In 6 cases subhyoid pharyngotomy was performed. Nearly all these 19 cases terminated fatally; but one patient, a woman of 45, was alive and well 5 years after the removal of a deep-seated malignant growth through a pharyngotomy opening. C. L.

NEUROLOGY

Plaut, F., u. **Steiner, G.** Recurrensinfektionen bei Paralytikern. [**Treatment of general paralysis by inoculations of the spirochaete of relapsing fever.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.* (Orig.), 1919, **53**, 103.

The authors have attempted to influence the course of general paralysis by producing a secondary infection with the spirochaete of relapsing fever, and then giving a course of salvarsan treatment in the hope that some active substance might be liberated from this by the action of the inoculated spirochaete. Eight cases, all more or less advanced, were thus dealt with. There appears to have been no definite clinical improvement, nor were the reactions of the cerebrospinal fluid favourably modified. G. de S.

Hamill, R. C. Encephalitis with involuntary movements. *Arch. Neurol. & Psychiat.*, 1920, **4**, 44.

Case I. Boy of 11. Pain in right half of face for ten days, vomiting for three days. On admission, fever, delirium, toxaemic appearance, signs of cerebral irritation and convulsions. No paralysis. Severe pain in right half face. 1,500 cells to c.mm. in cerebrospinal fluid. For six weeks he remained febrile, irrational, and incontinent. He then became rational, regained sphincter control, the cell count fell to 20 per c.mm., and there appeared persistent jaw clonus, frequent clonic spasms of abdominal muscles, diaphragm and thoracic muscles, occasional twitching of various groups of limb muscles, the rate being about 50 to the minute. In addition the tongue showed two kinds of tremor, and there was a twitching of the eyebrow of 80 per minute. These clonic spasms persisted after the general condition had become normal.

Case II. Man of 45. Sudden onset of intense pain down right arm, then down left. Clonic movements of both arms and of abdominal muscles on the third day of illness. Simultaneously delirium and fever. Leucocytosis and slight albuminuria. Only 10 cells per c.mm. in cerebrospinal fluid. Toxaemic condition persisted for several weeks, and there was pulmonary oedema and hypostatic congestion of the lungs. There was gradual lysis, and finally paresis of right arm and clonus of abdominal wall alone remained.

Case III. Woman of 20. Sudden onset of severe pain left side of neck and left limbs. Simultaneously intense tremor of left arm. No fever.

On admission. Muttering delirium, outbursts of screaming. Clonus of various muscles of respiration and of some limb muscles, rate about 50 to the minute. No other definite signs of organic nervous lesion.

Case IV. Man of 48. Sudden lancinating pain of vertex three days after blow on head. No details of first three weeks of illness. When seen clonus of sternomastoids, trapezii and erector spinae in cervical region. More marked during sleep and when awake patient is described as being unconscious of it. No other signs of organic nervous lesion.

All the patients appear to have recovered. Hamill regards them as similar to Sicard's 'acute myoclonic encephalitis'.

The paper contains some graphic records showing the rhythm of the clonus and its relation to the respiratory movements. Hamill believes that these show that the rhythmical movements arise from the activity of some medullary centre.

F. M. R. W.

Cadwalader, W. B. The condition of a patient in good health, but exhibiting automatic movements of the lower limbs, nineteen years after complete transverse section of the spinal cord by a gunshot wound. *Arch. Neurol. & Psychiat.*, 1920.

A remarkable case of survival nineteen years after total transection of the cord at the ninth thoracic segment. There is no similar instance on record of such prolonged survival and the case is therefore of some interest, in view of recent work on this subject. Unfortunately the report, taken from the Proceedings of the Philadelphia Neurological Society, is brief and in some respects incomplete.

In 1901 the patient, a young woman of 26 at the time, was hit in the thoracic spine by a revolver bullet. There was complete palsy and loss of sensation below the waist at once. Laminectomy was performed three hours later, and it was seen that the cord in the region of the ninth thoracic segment was completely divided and the severed ends were about an inch apart. They were approximated by sutures and the wound closed. From a contemporary account it appears that the condition now recognized as spinal shock was present for three weeks, after which a knee-jerk was obtainable. From the seventh week onwards involuntary flexion movements of the legs were present, and gave rise to the erroneous idea that suture of the cord had been followed by return of function, in fact, the case was published in 1902 as an example of recovery of function.

Examination in 1920 shows absolute paralysis of the musculature below the level of the tenth thoracic spine. There is no wasting of the legs, the muscles of which are said to show a flexor hypertonicity and lie in the flexed position. This rigidity is extreme, though in the prone position the legs can be extended by the observer, and then remain extended until some stimulus to the limb evokes a flexor spasm. Ordinarily, the patient sits up in a chair, and unless the legs are moved or otherwise stimulated there may be no flexor spasms for hours, but stimulation produces violent spasms in which there is flexion at hip and knee and dorsiflexion at ankle and toes. It is stated that no tendon-jerks can be obtained on account of the rigidity, but the jerks tested are not named. There is total sensory loss below the level of the lesion. The skin of the legs pits slightly on pressure, and is waxy in appearance.

The bladder empties automatically at definite intervals. There is no detailed information about the flexion reflex or any accessory reflexes.

The condition does not appear to differ materially from that now known to obtain in man after emergence from 'spinal shock'. The condition of paraplegia inflexion seems to have persisted throughout the nineteen years, and there has been no return to the extended type of paraplegia. Thus, the conclusions as to the nature and form of spinal activity in 'spinal man' formulated in this country since 1914 are borne out by this case.

F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Loeb, Leo, and **Hesselberg, Cora. Studies on compensatory hypertrophy of the thyroid gland. II. (a) Hypertrophy in autotransplants of the thyroid gland. (b) Does a deficiency in organ function influence the transplantability? (c) Hypertrophy in multiple transplants of the thyroid gland.** *J. Med. Research,* 1919, **40**, 265.

The authors here report further researches into the fate of transplanted thyroid gland tissue in guinea-pigs.

For their conclusions they rely solely on histological changes in the tissues interfered with. The histological changes signifying hypertrophy in the thyroid gland are stated to be:—Disappearance of colloid; granulation and swelling of epithelial cells tending to fill lumen of acini; formation of papillae in acini.

Autotransplantation of one lobe, leaving the other intact, produces no thyroid hypertrophy. In autotransplantation of one lobe of a completely extirpated thyroid, hypertrophy of the thyroid was observed in 26 out of 41 guinea-pigs. Mitoses were observed in the thyroid cells most commonly up to 16 days after operation, whether hypertrophy was present or not, and are regarded as of a regenerative character. They are more frequent in transplants than in remnants. Hypertrophy increases the mitoses for a few days after the 16th day following operation.

In experiments on fifty-six guinea-pigs it was observed that hypertrophy occurs in the autotransplant in practically the same percentage of cases as it occurs in the remnant *in situ* of an almost completely extirpated thyroid. In 16 of these both remnants and autotransplants were examined, and in 12 the conditions were almost identical; in 3 the hypertrophy was more marked in the remnant; in 1 the contrary was the case. In two guinea-pigs, only a few weeks old, but slight hypertrophy was observed, so it is concluded that there is no direct proportionality between age and liability to hypertrophy.

Hypertrophy was weak in two pregnant animals. The fate or success of the transplant is not affected by the presence or absence in the body of a deficiency in the internal secretion supplied by the gland. It is assumed that hypertrophy takes place as the result of a physiological deficiency in function, and in 16 animals examined the histological changes in the transplant were practically the same whether hypertrophy was present or not.

In each case there are three layers found in the 'healing-in' of the transplant. (1) An outer ring of thyroid tissue. (2) An intermediate zone of oedematous connective tissue produced as the result of body fluids bathing an ingrowth of blood and lymph vessels into (3) the inner central fibrous zone.

In homoiotransplants, there is much less efficient vascularization, as zone (2) is absent and zone (3) remains unchanged, whereas in autotransplants, which differ in metabolism from homoiotransplants and have a more stimulating effect on the formation of blood and lymph vessels, the rarified vascularized connective tissue zone eventually practically replaces the central fibrous nucleus. Non-hypertrophied autotransplants were found unabsorbed and well preserved as late as almost two months after transplantation.

Moreover a surplus of thyroid tissue was supplied by giving autotransplants and also syngenesio-transplants from a child to a mother which had previously been deprived of almost its whole thyroid. The consequent presence or absence of thyroid hypertrophy did not affect the course of the tissue changes in the transplants.

These multiple transplants had the same fate as single transplants under similar conditions. W. W. W.

Dolley, D. H., and Guthrie, F. V. The pigmentation of nerve-cells. II. The lipochrome a plant carotinoid pigment. *J. Med. Research*, 1919, **40**, 295.

The authors have shown in a previous paper that a melanin pigment is produced in nerve-cells by continued functional depression and is of nuclear origin.

In the present work they deal with lipochrome in nerve-cells.

Palmer and Eckles have recently (1914–1915–1916) pointed out that the natural yellow pigments in the fat of the lower animals (they work mainly on the cow and the hen) are exogenous, coming from the carotin and xanthophyll pigments in their food. They call the lipochrome of plants carotinoid. Escher showed that lutein is identical with carotin, in spite of its unsatisfactory reaction with Lugol's solution and sulphuric acid—the usual tests for plant lipochrome. The present authors rely rather on physiological feeding experiments. Professors Palmer and Kempster, of the Agricultural Experiment Station and the Department of Poultry Husbandry of McGill University, supplied them with the information that Leghorn fowls fed on a carotinoid (xanthophyll) free diet from birth develop colourless fat and lay colourless eggs; but these fowls when given carotinoid diet develop coloured fat and lay eggs which, with suitable feeding, are coloured normally or to excess (for the 'fancy' trade). So the authors fed six chickens with carotinoid-containing and six with carotinoid-free diet. Three chickens of each set were also subjected to depressing influences, varying in individual cases from beri-beri-inducing diet, heat, morphia poisoning to phosphorus poisoning.

The chickens with carotinoid-free diet, whether under normal or depressed conditions, showed no pigment.

Those with carotinoid-containing diet developed yellow pigment in the nerve-cells. The pigment was most abundant in the chickens of the depressed group. It occurred in any nerve-cell of any region, but especially Gasserian and spinal ganglia, and less in the stem and least in the cerebral and cerebellar cortex. It gave an adaptation of Palmer's modification of the Moore test, as used in dairy practice, depending on the fact that the pigment loses its colour on oxidation with ferric chloride, the latter turning green.

This was applied to frozen sections of fresh tissues, as formalin fixation obscures fine fat and lipochromes. In the carotinoid-fed chickens, ganglion pigment and also sections of skin and of carrot as a control were decolorized. The second phase (the green colour) of the test was more usefully employed as a gross test by treating a carbon disulphide extracted residue of the brain. The carotinoid-fed chickens gave a strong test, and the chickens fed on the carotinoid-free diet showed a trace of pigment; this latter result upholds Palmer's finding that it is not yet possible to produce a chicken without a faint trace of xanthophyll. The pigment gave Hueck's hydrogen peroxide test for his 'lipofuscin'. It gave all the usual microchemical reactions described for nerve-cell lipochrome, 'abnutzung' or 'fat holding pigment'. It was stained by scarlet red, Sudan III, and osmic acid. It gave a most beautiful result with Nile blue. It was dissolved easily by the usual fat solvents.

So the conclusion is that the lipochrome of the nerve-cells is a plant carotinoid or true lipochrome (the term lipochrome was originally used in respect of plants). The authors also hold that, certainly for the nerve-cells and probably for the somatic cells generally, Lubarsch's (1902) conception of the so-called 'fat-holding' pigment as an 'abnutzung' (wear and tear) and metabolic pigment is shattered. It is an exogenous pigment, incorporated in the cell. It is limited to such species as carry carotinoids in the blood-serum, e.g. it occurs in chicken, cow, and man, but is absent in the dog, rabbit, and swine.

Lipins (fat substances) in small quantities may be mistaken for lipochrome. As lipochrome is shown to be carotinoid, then lipins and lipochrome must be 'entirely miscible'; there is neither a fat-holding pigment nor a pigment-holding fat. Lipochrome alone is plain yellow, angular, amorphous; lipochrome in lipin is a globule, doubly refractive, tinged yellow; lipin in an excess of lipochrome has a globular form, but is yellower than the last.

Nile blue stains the lipochrome blue and does not stain the lipin, and its known salmon-pink staining of neutral fats failed in the nerve-cells, destroying the hopes of its being a differential between pure lipochrome and pure lipin.

But little melanin was found in the depressed chickens. It is distinguished by its persistence after application of fat solvents, by its slower oxidation with hydrogen peroxide or ferric chloride, and by its silver nitrate reduction. W. W. W.

Akaiwa, Hachiro. A quantitative study of wound-healing in the rat. I. Cell movements and cell layers during wound-healing. *J. Med. Research*, 1919, **40**, 311.

Loeb, Addison, and Spain, have shown that normal and regenerative growth of the epidermis differs markedly in various species of animals, and have pointed out the relationship between the variation in structure of epidermis and its proliferative energy. Further, working on the guinea-pig, Loeb and Spain have shown that the larger the wound the more rapid the growth of epithelium; that the movement of the epithelial cell determines its proliferation; and that the pressure at the meeting point of the ingrowing epithelial masses is a factor in the cessation of epithelial proliferation.

On the suggestion of Dr. Loeb a comparative investigation was undertaken by the author on the rat. Wounds of the ears only of rats were studied. The wounds were produced by trocars of 2 and 4 mm. diameter, and by razors producing wounds of similar diameters. The epidermis and tissue varying in depth up to perforation were removed. Wounded sites were removed at 2, 3½, 5, 7, 9, 11, and 14 days after operation, fixed in Zenker, cut 8 μ thick by the paraffin method, and stained in haematoxylin and eosin.

The author gives extensive measurements of the normal epidermis of the rat's ear; it varies from one to three layers of cells thick. After a description of the various changes in the proliferating epidermis, there is a long detailed account of the measurements of the length of the tongue of regenerating epidermis at different times after operation, divided into four series according to the nature of the wounding instrument and breadth of tissue removed. The variations according to the depth of the wound are also described. These figures of the quantitative determination of the rate of epithelial movement are again set out in a table, with measurements in millimetres to four places of decimals.

This is followed by a similar account of the changes in the number of epidermal layers and in the thickness of the stratum germinativum in the four series, both in the various parts of the epithelial tongue and in the border of the wound, accompanied by three tables of measurements.

The conclusions are that closure of a wound is brought about by (1) epithelial movements, (2) cell proliferation, and (3) contraction of the wound. It is stated, however, that the wounds under discussion showed rather relaxation, no contraction occurring until the wound was closed. The finding of Elsie Spain of pre-closure contraction in wounds of guinea-pigs is somewhat curiously included as a conclusion of, as well as contradicted by, this work.

Further conclusions are, that largeness of a wound stimulates growth of epithelium, the larger wounds, therefore, closing relatively more rapidly than smaller wounds.

Shallow wounds close more quickly than deeper ones, because of resistance offered to the epithelial growth by 'the unfavourable character' of the surface of the deeper wounds.

Epithelial movements and proliferation occur in the epithelium bordering on the defect, as well as in the covering tongue.

W. W. W.

Akaiwa, Hachiro. A quantitative study of wound-healing in the rat. II. Cell growth during wound-healing. *J. Med. Research*, 1919, **40**, 371.

In this second communication the author deals with variations in the epidermal cells in wounds of different size and depth with regard to number of mitoses, increase in size of cell and nucleus, and number of layers of epithelium.

There is first set out and discussed at great length the variations in the number of mitoses in the three important areas of the epidermis bordering on the defect. These areas are: the insertion of the tongue and the zone one mm. and the zone two mm., from the edge of the defect. There is a similar description for the three divisions (base, middle, and tip) of the new epithelial tongue. These variations are discussed separately for five series of wounds, namely, the 2 and the 4 mm. trocar wounds, and the 2 and the 4 mm. razor wounds, and the 2 mm. trocar wounds with perforation. The results are again set out in two tables.

Next the changes in size of epithelial cells and nuclei are dealt with in the same way, and this part is supplemented with three tables.

Lastly there is a similarly arranged description of the variations in the number of living cells in the stratum germinativum, and the figures are given again in two tables.

The results are separately and collectively summarized.

The number of mitoses, as well as the number of living cells, in the epithelium, indicating its proliferative power, both increase in the three zones above mentioned bordering on the defect up to the time of closure of the wound.

Soon after closure the number of mitoses in this old epithelium falls sharply and the number of cells more gradually. In the new epithelial tongue the number of mitoses is small in the first few days. Corresponding with the sudden fall in the number of mitoses in the old epithelium there is a rise in the new epithelium, suggesting a certain equilibrium between the two. The mitoses return to normal numbers in both about 14 days after operation.

There is a greater mitotic proliferation in both old and new epithelium in larger than in smaller wounds. This increase and the increase in cells extends for a larger area in the old epithelium in larger wounds than in smaller wounds. In the latter half of wound-healing the number of mitoses and of cells is greater in deeper than in shallower wounds, and at all times is greater for perforating than for non-perforating wounds. The increase in size of cells goes hand in hand with the mitoses.

W. W. W.

Foot, N. C. Studies on endothelial reactions. The macrophages of the loose connective tissue. *J. Med. Research,* 1919, **40**, 353.

This paper relates an experimental attempt to establish the identity and origin of the macrophages of the loose connective tissue, the cell or cells called ‘large mononuclear cell’, ‘endothelial cell’, macrophage’, ‘wandering connective tissue cell’, &c.

The author points out that he based his experiments on a combination of the results of various similar researches, especially those bearing on the absorption by the macrophages of benzidin dyes and certain inert substances, during the life of the animal—vital staining. McJunkin is quoted as finding that cells of endothelial origin can be labelled by the use of a colloidal lampblack-gelatin solution. The author started with the assumption, based on the researches he mentions, that if the mononuclears were of omental or connective tissue origin they would stain with the benzidin dye; if endothelial, they would ingest the lampblack.

So he tried a combination of trypan blue intraperitoneally and lampblack intravenously with agar subcutaneously to induce a reaction. A guinea-pig saturated with trypan blue showed it only in small amounts in the foreign-body syncytia developed round the agar mass which had been injected twelve days before examination. Next, a series of mice failed to provide a reaction to the agar sufficient for study.

The third experiment, on which this paper is largely based, was done on a large white male rabbit. Being kept saturated with trypan blue (10 c.c. of a 1 per cent. solution almost every day) it was given daily injections of 1·5 to 2·0 c.c. of an emulsion of 5 per cent. lampblack with 1 per cent. gelatin in normal saline. Subcutaneous lesions of varying ages were obtained by daily injections of melted sterile agar into the skin of the back, up to the 13th day, when the animal was killed. Intramuscular lesions were also induced on some of these days.

Blood smears showed lampblack granules in 70 per cent. of the circulating mononuclears. In sections moderate amounts were seen in the general vascular and lymphatic endothelium. The cells of the omentum were stained with trypan blue and were often loaded with lampblack. Endothelial cells of the lungs, and of the sinusoids of the liver and the spleen, were loaded with lampblack.

Mononuclear cells found in the agar lesions are divided into two types, (1) a compact, dense cell with opaque cytoplasm and bean-shaped nucleus (average 7 μ), and (2) a large, vacuolated, mononuclear, the 'clasmatocyte' (7·5 by 12 to 15 μ). The former contained no trypan blue, but one-third of them contained lampblack; the latter contained both. The vascular endothelium in the lesions was proliferated and contained lampblack granules. The state of the mononuclears is described in the lesions of various ages. They begin to form syncytium on the third day. Migration of mononuclears almost ceases on the seventh day. Mitoses are found in those which have migrated, especially when there is no further migration. With division of the cells, lampblack granules become more sparsely distributed, no new carbon being brought in.

Another rabbit was used to perform the oxidase test, and also to determine at what period the endothelium took up the lampblack. It was given in the same way, agar and lampblack, and then again lampblack the following day, and killed ten days after. In frozen sections the polymorphonuclears gave the oxidase reaction, while the endothelial cells in the lesions and the syncytia were free from oxidase granules. Most of the discrete endothelial cells and all the endothelium still lining the vessels were free from lampblack, but those that had by this time become syncytium contained lampblack. Evidently the endothelium takes up the lampblack at or just before its migration.

It is claimed that, as the endothelium of the vessels and the circulating endothelial leucocytes contained carbon, the migrating carbon-containing mononuclears come from one of those two sources; that the source is not the circulating cells only (as McJunkin suggested), because 70 per cent. of the latter contained carbon and only 30 per cent. of the migrated cells contained it. Further, there is no increase in the percentage of circulating mononuclears and there is no proliferation of vascular endothelium generally, but there is a swelling of the endothelium near the agar lesions. Therefore, it is concluded that the phagocytes or macrophages of the loose connective tissue of the rabbit are of endothelial origin; that they probably come from the vascular endothelium near the lesion, not entirely from the circulating mononuclears; and that they do not originate in the omentum, connective tissue cells, or lymphocytes.

There is a somewhat rambling discussion of the views of other workers. The evidence set forth in the paper is meagre. There are four drawings which are not very helpful. W. W. W.

Oertel, Horst. The essential atrophy of the pancreas. *J. Med. Research*, 1919, **40**, 289.

Dr. Horst Oertel writes a short account of the condition in the pancreas to which he gives the above name and which he regards as an entity. He has recorded several cases in a previous publication.

He has seen four cases in the last five years and has records of another. They occurred in three males of ages 22, 32, and 33 years, and two females of ages 32 and 54 years. The disease is associated with acute diabetes, coma, and death.

The pancreas is diminished in size and weight. In the five cases it varied from 35 to 120 grm.

Microscopical pictures are uniform. Interlobular septa are atrophied, losing fat and leaving wide spaces. The lobules are small and condensed. The acini are small. The acinar epithelium is found in various stages of cell atrophy, nuclei remaining distinct until late. This ends in loss of acinar outline. The atrophy is associated with aborted and atypical regenerative activity of parenchyma. Small cells of multinucleate syncytial masses are found in foci of advanced atrophy, lying diffusely in an unorganized faint matrix. Blood-vessels and larger ducts show no change. Islands of Langerhans may disappear, and then 'independent structural changes never occur'. Occasionally, the cells of the islands undergo hyperplasia of an atypical embryonic type. There is absolutely no trace of round-celled or fibrotic inflammatory reaction.

This lesion is therefore regarded as an unco-ordinated pathological exaggeration of the normal physiological process of acinar collapse and reconstruction which is constantly (as first noted by Reitmann and confirmed by Oertel and C. M. Anderson) going on in the pancreas.

W. W. W.

Parker, F. (junior). Toxic necrosis and regeneration of the acinar cells of the pancreas. *J. Med. Research*, 1919, **40**, 471.

Happening to find a mitotic figure in a pancreatic acinar cell, the author proceeded to investigate the frequency of necrosis and regeneration in these cells. He classifies types of necrosis in the pancreas thus:

1. Acute pancreatitis with fat necrosis.
2. Necrosis due to toxins, similar areas to those found in the liver, &c., and claimed to be now for the first time described in the pancreas.
3. Infectious pancreatitis—due to infection by organisms along the ducts (leaving nothing to chance the author stimulates the reader's comprehension of this phenomenon by stating that it is 'similar to infectious cholangitis and pyelonephritis'), or by infection by the blood-stream or by direct extension.

Regeneration of acinar cells was found associated with the toxic necrosis. Mitotic figures were found in 100 pancreases from cases dead of various bacterial or protozoal infections of the body (tabulated). Seventeen of these were cases of 'suppurative processes elsewhere in the body due to the streptococcus, pneumococcus, rarely *Staphylococcus aureus*'.

The first microphotograph is a picture of an area of intense purulent infiltration of the pancreas; it would be indeed surprising not to find necrosis of acinar cells here. This picture is described as 'toxic necrosis of acinar cells in a case of late scarlatina and septicaemia (? of streptococcus)'.

Presumably, the author's search for organisms in this pyaemic-looking lesion was unsuccessful. The other microphotographs are stated to show toxic necrosis, mitotic figures, and phagocytosis of necrotic cells by endothelial leucocytes. None of these features can be identified.

Other organs were examined for necroses. The organs are placed in the following order as regards frequency of this lesion in them: adrenal, pancreas, liver, and heart.

Experimental work in this research is represented by the finding of degenerations, regenerations, and necrotic débris in the liver, adrenal or pancreas of one chloroformed guinea-pig and of one aborted guinea-pig which had received *per os*, a dose of liquor potassii arsenitis. W. B.

Loeb, Leo, and **Fleisher, Moyer S. The growth of tissues in the test tube under experimentally varied conditions, with special reference to mitotic cell proliferation.** *J. Med. Research*, 1919, **40**, 509.

This is a long report of the further investigation by these workers of the growth of tissues in culture media. They now pay special attention to mitotic cell proliferation in cultured tissues and its variation with varied conditions.

There is an account of their experiments, which are in thirteen series, each series comprising many different experiments. An occasional complete abstract of an experiment is given, as an example, with exact number of mitoses found in each piece of tissue, &c. Pieces (size not specified) of various tissues were embedded in the media and afterwards cut in serial sections, sections being also made of control portions. The central part of a cultivated piece becomes necrotic while the peripheral part may live and cells from it invade the medium. The only difference from transplants *in vivo* is that the dead centre in culture is not invaded by granulation tissue, probably owing to difference in oxygen supply. Varying conditions were introduced by filling some culture tubes with air, standing others in a container full of hydrogen, supplying others with oxygen either continuously or at short or long intervals.

Similar experiments in the same series did not always give the same results. This suggests the presence of factors not yet understood, such as variability in the power of proliferation or resistance possessed by the tissues of different animals. In addition to normal tissue they used tissue that had been wounded five to nine days previously, thus introducing the effect of existing processes of regeneration.

Normal rabbit kidney, wounded kidney with capsule, and mouse carcinoma were immersed in rabbit plasma coagulum under varying gaseous conditions.

Mitoses were found in epithelium of simple tubules and in the 'epithelial cell layer covering the surface of the kidney and the coagulum'; also in connective tissue cells, especially those which have entered or are near the coagulum, and also in those of the capsule of the kidney. Mitoses were on the whole more numerous in epithelium than in connective tissue. A mitotic division was also found in the nuclei of these cells, with an occasional giant cell in a tubule. Epithelial cells of convoluted tubules usually die. Blood and lymph vessels merely survive; they do not proliferate. Most mitoses and a larger area of living tissue were found with a supply of pure oxygen. Air, even when washed through a purifying mixture, was not so beneficial. This difference was marked under nearly all conditions.

Tobacco smoke mixed with the oxygen only sometimes caused a diminution in number of mitoses. In an atmosphere of hydrogen the tissues died. Regenerating kidney (with healing wounds) provided as a rule more live tissue and more mitoses in epithelium and fibroblasts. This difference, which was by no means marked or constant, is explained by the more active vitality of the simpler, less complicated elements of the regenerating tissue. Varying the osmotic pressure within limits, by adding isotonic Ringer's solution, water, and hypertonic solutions to the plasma, produced no marked alteration in mitoses or outgrowth.

Addition of KCN solution diminished mitosis, but it took a somewhat strong solution, equal parts of 1/10 per cent. KCN and plasma, to cause cessation of mitoses.

Addition of very weak alkali seemed to increase the mitoses, probably by neutralizing acid products of tissue metabolism.

More mitoses were found in connective tissue cells that were migrating into the medium than in others deeper in the tissue.

Rabbit's serum used as a medium instead of plasma, being more fluid and having no coagulum fibres, prevented outgrowth of cells, and under these circumstances mitoses in cells were fewer. The authors therefore consider that the migration or movement of connective tissue cells occurs as a response to the stimulus of altered environmental conditions, and that the mitotic proliferation is a response to the migration which acts as a secondary stimulus.

In epithelial cells no such relation between proliferation and migration was made out, although in Akaiwa's work in this journal there is evidence that there may be a certain relation in some cases.

Similarly, coagulated blood used instead of coagulated plasma is denser by the presence of red blood corpuscles and produced diminution in outgrowth of fibroblasts, and here again mitoses were fewer in fibroblasts, but here the mitoses were reduced, probably also by retardation of diffusion of oxygen through the thickened medium.

In mouse carcinoma in coagulated plasma mitoses are more numerous in carcinoma cells than in stroma cells, whilst amoebic outgrowth into the medium takes place on the part of the stroma cells more than mitoses—two cells reacting differently to the same stimulus.

Stereotropism directs movement and direction of proliferation of cells. Fibroblasts (and probably also other cells) move along fibres and their mitotic axis is parallel to these fibres. Migration is only possible with favourable direction of fibre. Thus direction of fibre in the coagulum directs mitotic proliferation.

Outgrowth of cells into the medium is not a reliable indication of life or activity in the cultured tissue, as outgrowth may be absent, and yet the piece may be well preserved and actively growing.

A yeast isolated from a human cancer was injected intravenously into a rabbit, and the rabbit's kidney in which the yeast grew was implanted into plasma with air supply. The yeast did not prevent, but probably diminished, fibroblastic outgrowth and mitotic activity.

Many experiments were done to determine time limits of mitoses in cultures. It was found that the maximum number usually occurred three days after transplantation; after four or five days the tissue began to deteriorate. In oxygen a greater number of mitoses may still be found at five days, but oxygen cannot prevent deterioration. At seven days proliferation is no longer observed. Deficiency in removal of products of tissue metabolism account for this difference from growth *in vivo*.

Further experiments showed that rabbits' tissue grew in rats' plasma and vice versa. Both mitoses and phagocytosis may occur in heterologous plasma. In cultivated rats' and rabbits' thyroid the colloid disappears and the connective tissue becomes necrotic; the acini survive and a few mitoses are found. Testicle showed activity of stroma cells; spermatozoa were not produced. In cultivated ovary small follicles, germinal epithelium, and tunica albuginea survived and mitoses were found in the germinal epithelium. Portions of uterus, in some cases infected with cocci, dissolved the coagulum and did not usually show mitoses or outgrowth. Heart, aorta, ureter, and two different rat sarcomata showed little vitality and were usually found necrotic. W. W. W.

Loeb, Leo. Further investigations on the origin of tumours in mice. VI. Internal secretion as a factor in the origin of tumours. *J. Med. Research*, 1919, **40**, 477.

An adenoma of a rat's breast, on being transplanted into the same animal, grew during the pregnancy of the animal like the normal mamma and the original adenoma. Its proliferation ceased at the conclusion of pregnancy and was even followed by retrogression. The same hormone evidently acted on mamma, adenoma, and transplant.

Similarly, with corpus luteum hormone and mechanical stimuli, temporary decidual tumours, like maternal placenta, were produced.

The late Miss Lathrop, the author's co-worker, observed the opposite effect, i. e. retardation of growth in spontaneous cancers in mice during the animals' pregnancy. Haaland and others found that the number of 'takes' and the growth energy in transplanted tumours are both diminished during pregnancy. This suggests that the growth-directing hormone acting on adenoma is not efficient in carcinoma. Goldziehen and Rosenthal found that castration in mice does not influence growth of homoiotransplanted carcinomata. Rohdenburg, Bullock, and Johnson found only a slightly retarded growth on removal of various glands previous to or following the inoculation of an homoio-tumour. They report, however, that injection of tissue extracts, especially thymus, has been observed to cure both mouse and human (Rohdenburg and Gwyer) cancers. On this statement judgement should be reserved.

Removal of ovaries in inoperable human mammary cancer has at best possibly produced retardation of growth in some cases.

Cancer, once developed, is not affected by ovarian hormones, but the latter may possibly affect the tissue changes which lead to the development of cancer in the breast.

The author, therefore, attacked this problem experimentally, using mice in which cancer rate and cancer age had been constant for generations, and especially strains in the first age period and in which the normal incidence of cancer was higher than 50 per cent. His results have been partly reported before.

One hundred and thirty-three mice survived castration long enough for the purpose of the investigation.

The results are stated with details of strains of mice and age of spaying. Records are also given of non-castrated controls of similar strains.

Of 54 mice castrated between ages of 3 and 6 months only one developed a tumour, whereas in the controls there were tumours in 56 per cent. to 80 per cent. Of those castrated between 4 and 7 months of age, there were 30 mice without tumours and 13 with tumours, i. e. a tumour rate of 30 per cent., compared with 60 per cent. in controls.

In those castrated at 7 to 10½ months there was no alteration in normal rate of tumour incidence.

It is therefore concluded that there is a hormone given off by the ovary which regulates those tissue changes which lead to the development of cancer of the breast in various strains of mice, and that the influence of this hormone is a quantitatively graded one.

Late castration does not prevent the development of even those tumours that appear in the third age period, suggesting that the tissue changes leading to cancer occur at an early period in life.

Further, it was found that castrated mice without tumours lived longer than controls without tumours.

Additional experiments on prevention of breeding are reported in this article. They confirm previous conclusions that prevention of breeding only slightly lowers tumour rate and raises the age of tumour incidence. Non-breeding mice live longer, so it is concluded that castrated mice live longer because they do not breed. Transplantation of ovaries to castrated males was done successfully on 19 mice. In seven only the transplanted ovaries (sometimes containing new corpora lutea) were recovered. In no case did cancer develop in the breast of these artificial females, although females of this strain dying at the same age would have shown a considerable incidence of cancer. Transplanted ovaries therefore do not function so well or so rhythmically as normal ovaries.

From the experiments the conclusion is also drawn that it is the ovarian hormone, and not the effect of pregnancy, nursing, or structural difference, that is directly responsible for the difference in mammary cancer rate in male and female mice. The hormone is specific; i. e., it influences cancer only in those organs to which normally it has a specific relation; e. g. breast and ovary, uterus and ovary, prostate and testicle. Final conclusions are that heredity, irritation (physical stimulation), and internal secretion (chemical stimulation) are the main factors active in the development of cancer. That the heredity and internal secretion act together; that the heredity factor may be associated with irritation; but that the latter by itself, if great enough, is sufficient to cause cancer.

W. W. W.

Berry, Frank B. Report of three cases of combined tumours of the kidney in adults. *J. Med. Research*, 1919, **40**, 459.

This is a short description and discussion of three cases of an interesting and unusual tumour, which differs from the mixed renal tumours of children.

The first case, a woman aged 43, had a history suggesting development of the tumour over a period of more than six years. It was the 'size of a head', encapsulated, with thin remnants of renal tissue under the capsule, and composed of hard tissue-like cartilage and small soft reddish-brown areas. With the microscope there were seen to be two elements in the neoplasm: a rapidly growing sarcoma with large long cells, giant cells, and collagen fibres; and also an adrenal cell carcinoma (Grawitz's tumour) with large pale polygonal cells; in places sarcoma and carcinoma were intimately combined. The patient did not rally after the operation and there was no autopsy.

The second tumour, in a woman aged 35, who had noticed a lump for one year, was an encapsulated whitish mass about the same size as the first. The microscopical picture was: a very cellular spindle-celled fibrosarcoma and a papillary tubular adenocarcinoma of the type of a carcinoma arising from renal tubular epithelium. Patient died eight days after operation and there was no autopsy.

The third, in a male aged 72, was a somewhat smaller tumour in the upper pole of the kidney. It was composed of an adrenal cell carcinoma and a leiomyosarcoma.

The patient recovered, but there is no further account of him.

There have been but four of these cases in the author's laboratory in 20 years.

There is a short discussion of the various opinions as to the nature of the Grawitz tumour: (1) The old-fashioned view that it is a sarcoma, simply because of its origin in a mesoblastic tissue. (2) Grawitz's idea that it was an ectopic hypernephroma. (3) That it is an epithelioma arising from the epithelium of renal tubules or regeneration of nephrogenic tissue.

It is concluded that the three tumours reported in this paper are not true mixed tumours with the two parts interlacing throughout as in the mixed parotid tumour, for the two parts are quite distinct and each has its own stroma. Neither are they cases of sarcoma arising by the stroma of a carcinoma becoming malignant, but that they represent a true combination of two tumours, epithelial and connective tissue, similar to the combined epithelial and sarcomatous tumours of the breast.

The paper is illustrated by six excellent photomicrographs.

W. W. W.

Graves, Stuart. Primary lymphoblastoma of the intestine. Report of three cases, one with apparent recovery following operation. A plea for a logical classification of tumours. *J. Med. Research*, 1919, **40**, 415.

This is a report of three cases of the intestinal condition usually known as lymphosarcoma, to which the author gives the name of lymphoblastoma.

The author appeals for the universal adoption of an intelligent and scientific nomenclature of neoplasms. A classification based on histological structure, the only such classification at present possible, is advocated. It is, however, surprising to find at the end of this plea the following statement: 'The term "sarcoma" should be applied only to those tumours whose type cells arise from the mesenchyme. . . .' It does not require a very extensive acquaintance with tumours to afford a meeting with an example which renders this purely embryological definition of 'sarcoma' untenable.

In 13,036 autopsies at Prague there were only 13 cases of lymphosarcoma of the intestine. The author's search of the literature revealed only 246 cases of lymphoblastoma of the intestine. He found great difficulty in selecting cases owing to confusion in the nomenclature. To the article is appended a 2½ page bibliographical list. Crowther's collection from the literature of about 120 cases of lymphosarcoma, out of a total 191 cases of sarcoma of intestine, was the largest previously recorded.

The disease is most common in the third and fourth decades of life, and is found in males about three times as often as in females. It affects any part of the intestine, but most commonly the lower ileum. Perforation of gut is rare. Aneurysmal dilatation of the affected part may occur and the suggested explanation of this is paralysis of intestinal muscularis from infiltration. Constriction sometimes results from fibroblastic stimulation. 'Eosinophils have nothing more to do with the nature of the tumour than they have in the so-called Hodgkin's disease or in carcinoma of the cervix uteri.'

Recurrence may not occur for years after operation, but death is the usual outcome. It is interesting to note that the microscopical description of the author's first case (specimen obtained at operation on a male aged 54) is that of a granulomatous inflammation. That he evidently recognizes this is admitted by his guarded diagnosis: 'No evidence of carcinoma or tuberculosis. No positive evidence of tumour. Possibly a very scirrhous lymphoblastoma.' There were great numbers of eosinophil leucocytes in the lesion. The patient died with signs of metastases, but there was no autopsy. Only a single large (15 cm. in greatest diameter) lesion was seen. It involved the lower ileum and caecum. Mesenteric glands were small and firm.

The second case (male aged 40) supplied from operation 3 feet of upper small intestine in which there were seven focal areas of lymphosarcoma (the largest 7 cm. long and 1 cm. thick) as well as numerous minute nodules. The lesions were composed of small round cells like small lymphocytes and less differentiated cells, larger, paler with more cytoplasm and paler nuclei. There were also eosinophil leucocytes. The stroma was scanty. After 38 months of good health the patient reported with signs and symptoms of abdominal recurrence, and no further record is given.

From operation on the third case (female aged 15 years) was obtained a specimen consisting of caecum, lower ileum, and ascending colon. There was a slight intussusception of the ileo-caecal valve into the colon. There was a polypoid, grey, soft, homogeneous growth (10 by 6 cm.) projecting into the colon, and a plaque (5 by 3 by 1·2 cm.) in the ileum. The cells forming the tumours were lymphocytic in type, many of them immature and resembling 'lymphoblasts' of the germinal centres. There were few eosinophils and scanty stroma. The mesenteric glands were enlarged (up to 4 by 5 by 6 cm.) and similarly infiltrated. The patient was in good health three years after operation.

The article is illustrated by ten macroscopical and microscopical photographs.
W. W. W.

Alter, H. M. Histological changes in squamous cell carcinoma of the cervix of the uterus after radiation. *J. Med. Research*, 1919, **40**, 241.

After a foreword on the complexity of the problems into which such an investigation leads—'problems concerning the very nature of life itself'—the writer gives a useful account of the views of other students of the changes wrought in neoplasms by radium. Starting with the first of such publications by Exner in 1904, the author then gives us the opinions of Finzi, London, Wickham and Degrais, Dominici and Warden, Caan, Aschoff, Haendly, Bumm and Doederlein, Frank, Schottländer, and Ewing. These writers, while in many cases giving good descriptions of the changes in the malignant cells, tended to emphasize the part played by the contraction, 'and perhaps proliferation', of the fibrous tissue of the radiated growth. Thus Ewing says 'the best effects of radium do not consist merely in the killing of cancer cells but it may excite a slow and complex process in which stimulation of capillaries and fibroblasts is prominent'. Dr. Alter suggests that light will also be thrown by his investigation on the question as to whether the connective tissue (Virchow and Ribbert) or the epithelium (Hauser, Hansemann, Lubarsch, and others) is responsible for the primary aetiological move in carcinoma.

He expects to record in a series of papers the changes observed in various types (want of space precludes the description of the changes in each individual case) of malignant disease after radiation, using a material of about one thousand specimens. The present article is concerned with carcinoma of the uterine cervix, of which 275 specimens were examined, some of them from the same case at different times.

His technique was varied: routine 10 per cent. formalin and occasionally Zenker's fluid; routine celloidin and occasionally paraffin; haematoxylin with eosin stain and also iron haematoxylin (his favourite nuclear stain), safranin, thionin, cresyl, echt violet, and methyl green; dahlia, pyronin, safranin, water blue tannin, polychrome methylene blue washed by acid fuchsin tannin and Van Gieson's, Mallory's, and Weigert's fibrin methods.

There is an interesting summary of the writer's study of carcinoma of the cervix. It is impossible, however, to reconcile the following two statements, 'The so-called "squamous" carcinoma of the cervix is a basal-cell growth' and 'True pearls do not occur in basal-cell carcinoma', with the fact that there is not infrequently very extensive horny pearl formation in carcinoma of the cervix. He describes the multiple (microscopic) origin of the growth in the dipping down of gyri of basal cells, and proceeds to divide the growth into different types according to the characteristics of the further development of the gyri:

(1) An *adenoid type* composed of regularly branching gyri of cubical, oval, or cylindrical cells with stroma, which is often hyaline, filling the lumen seen in cross-section. This rather uncommon type resembles rodent ulcer.

(2) A *solid type* showing irregularly branching, smaller or larger, solid alveoli of larger, not so elongated, cells. 'True keratin pearls can never be found save when the growth derives from prickle cells.'

(3) A *cystic type* with solid and cystic alveoli, the cysts being formed by 'quasi-secretory degeneration of the central cells'.

A general description of the changes after radiation is then given.

During the first week after radiation there is an inflammatory reaction in the growth with a very intensive eosinophilia. Epithelial cells are separated by young blood-vessels, haemorrhage, and oedema.

After one week the changes in the parenchyma cells predominate. The chromatin substance of the cells appears most sensitive to the rays. There is increasing swelling of nuclei and protoplasm. The nuclei become uniformly pyknotic; this is soon followed by chromatolysis. The protoplasm gradually becomes strongly acidophil and progressively vacuolated. Interstitial eosinophil leucocytosis in association with the above changes 'suggests deep chemical destruction due to the rays of radium'.

After about the second week mitotic figures disappear. The connective tissue, so far inconspicuous, now appears increased, but its cells never show mitotic figures. It is formed mainly of wandering cells. Grouping of cancer cells disappears; they lie solitary, giving a sarcomatous appearance. Cancer nuclei swell up, become irregular, and lie eccentrically in protoplasm which tends to fuse into the surrounding homogeneous matrix. The connective tissue fibres are undergoing hyaline degeneration. Large, irregular, deeply haematoxophil, chromatin masses appear and can be seen, by studying intermediate stages, to be formed by the flocking together and fusion of cancer cells with dispersed chromatin. The nuclear substance is now in an unorganized state, obeying simple physical and chemical laws. These masses are surrounded by phagocytic cells and granulation tissue, and they gradually disappear, being eventually got rid of by polymorphonuclear leucocytes and mononuclear endothelial cells. Mast cells and plasma cells are numerous at certain stages. The remaining connective tissue becomes fibrous and scar-like. On the surface develops an eosinophilous substance from the dissolution of the cytoplasm. This is covered by a layer of haematoxyphil nuclear débris in globular masses or dust. These surface coverings are invaded by connective tissue from beneath. Repair is completed by regeneration of epithelial surface.

The author claims that, though the stroma is histologically transformed, there is no evidence whatsoever that it is stimulated to active growth by the rays of radium. The rays destroy the proliferating power of the epithelial cells and bring about their disintegration. Hence the balance of tension between epithelium and connective tissue is upset, and the connective tissue expands; the increase is secondary to destruction of parenchyma. This article is accompanied by one coloured drawing and eighteen microphotographs. W. W. W.

Ellermann, V. Beretning om en Stamme av Hönseleukose (Stamme, H.). [**Gallinaceous leucosis.**] *Ugesk. f. Læger*, 1920, **82**, 279.

Ellermann has succeeded in propagating a strain of gallinaceous leucosis through twelve generations. His virus was obtained from a living hen received in February 1917. With citrated blood from this bird he inoculated eight healthy hens intravenously. Only one of them contracted the disease. Altogether 122 birds were inoculated, with positive results in 34 (27 per cent.). Although the strain ultimately died out after the twelfth generation, its virulence was increased by passage, as shown by the decreasing duration of the disease. But this increase of virulence was not accompanied by an increase in the proportion of positive inoculations; 60 to 70 per cent. of the animals maintained their natural immunity. As in the case of other strains, it was found that this strain, too, gave rise to various forms of disease, i. e. myeloid, intravascular lymphoid, and (one case) lymphatic disease. In the intravascular lymphoid form there was a reduction of the haemolytic action of the serum on the erythrocytes of rabbits. This phenomenon was not observed in the myeloid form. Active immunization could not be achieved by subcutaneous injection of the virus, which proved, as in earlier experiments, to be filterable. Inoculation of hens with blood taken from human subjects of leukaemia yielded no positive results.
C. L.

Krumbhaar, E. B., and **Krumbhaar, Helen D. The blood and bone marrow in yellow cross gas (mustard gas) poisoning. Changes produced in the bone marrow of fatal cases.** *J. Med. Research,* 1919, **40**, 497.

In a previous paper one of the authors described the changes in the blood in this form of poisoning, of which dichlorethylsulphide is the chief constituent. The chief changes were an early leucocytosis followed by a leucopenia as low as 1,000. A white blood count of less than 5,000 was found to indicate a very bad prognosis. Two charts are given in this paper showing that the period in the duration of the disease of highest mortality coincides with the most severe leucopenia. The changes in the white count were variations in the polymorphonuclears, with disappearance of eosinophils in the acute stages, and temporary appearance of myelocytes; the latter sometimes formed as much as 90 per cent. of the white cells. Leucopenia seemed to be due to lessened blood formation.

Pappenheimer's experiments on rabbits confirmed these findings. Warthin found in experiments that pure dichlorethylsulphite produced no leucopenia, so the leucopenia may be due to other elements in the mustard gas. Miller and Hermann have not found the leucopenia in their cases.

The authors now present their study of the bone marrow in fifty-five fatal cases. A three-inch cylinder was taken from the middle of the right femur, fixed in Zenker, and cut by the paraffin method. Macroscopically, congestion often simulated cellular hyperplasia, so the actual portions taken for section perhaps sometimes gave false impressions. Also areas which to the naked eye were apparently hyperplastic would be found to be composed almost entirely of immature forms of cells, polymorphs and normoblasts being absent.

Details are given of 10 typical cases of varying duration of from 3 to 21 days, with clinical findings, blood counts, post-mortem findings, and histology of bone marrow.

Attempts at blood regeneration were considered to be absent in 14 marrows, slight in 28, and moderate in 13. Small areas of necrosis were found.

It is concluded that the gas has a direct toxic action on the bone marrow, because the changes are found in cases where infection was absent, and none of the known 'leucopenic' infections played a part in the cases.

The effect on the bone marrow interferes with the ability to resist secondary infection.

The article is illustrated by 11 microphotographs and 1 drawing, of marrow. W. W. W.

BIOCHEMISTRY

Thunberg, T. Zur Kenntniss des intermediären Stoffwechsels und der dabei wirksamen Enzyme. [**On intermediate metabolism, and the enzymes concerned therein.**] *Skandin. Arch. f. Physiol.,* 1920, **40**, 1.

It has long been known that emulsions of living cells decolorize methylene blue. This property is lost when the cells are extracted with distilled water. But it is restored when certain organic acids are added to the mixture of methylene blue and the emulsion of extracted cells, although these organic substances are by themselves unable to reduce methylene blue. A large number of organic acids were tested, but only a small number was found to possess this property of inducing the reduction of methylene blue in the presence of extracted cells. Such substances are, for instance, succinic acid, lactic acid, oxybutyric acid, malic acid, citric acid, glutamic acid. The specific nature of this reaction is exemplified by the fact that laevo-tartaric acid possesses this power, but dextro-tartaric acid does not.

The reaction is explained as being due to ferments which remove two hydrogen atoms from the organic acids and transport them to the methylene blue which is thus reduced. These ferments are called 'hydrogenotransportases'. The organic substances from which the hydrogen is removed are called 'donator substances'. Evidence is adduced to show that the ferments are specific for different donator substances.

The theoretical significance of these reactions is discussed in detail. It is pointed out that this reaction affords a convenient and very delicate method to identify the intermediate products of cell metabolism.

W. C.

Töttermann, U. Alcohol und Präcisionsarbeit. [**Alcohol and accurate work.**] *Skandin. Arch. f. Physiol.*, 1920, **40**, 107.

The observations were made on the author. The test work was the threading of sewing needles. The number of needles were counted which could be threaded in a given time (20 minutes). The amount of alcohol consumed was 100 c.c. of a 25 per cent. solution, i. e. 25 c.c. of absolute alcohol. This was taken at 11 p.m. The test work was done the next morning at 10 a.m., i. e. eleven hours after the administration of alcohol. The amount of alcohol consumed corresponds to that taken by a moderate drinker. But as the author himself points out, it was taken in a rather concentrated form and on an empty stomach. An alcohol free period of 14 days was followed by an alcoholic period of 10 days, this again by an alcohol free period of 9 days and an alcoholic period of 10 days.

The experiments show a distinct and progressive diminution during the alcoholic periods in the amount of the test work done. This was partly due to a diminished general capacity for the test work and partly to fatigue setting in more rapidly. It was noted too that during the alcoholic periods a trembling of the hands and a fatigue of the eyes developed while the test work was being done.

W. C.

Rancken, D. Das Verhalten der Körpertemperatur bei mechano-therapeutischer Behandlung und gymnastischen Freiübungen. [**The behaviour of the body temperature during mechano-therapeutic treatment and gymnastic exercises.**] *Skandin. Arch. f. Physiol.*, 1920, **40**, 92.

The paper is part of an extended investigation on the effects of certain movements on the fundamental body functions, such as temperature, carbon dioxide excretion, blood distribution and so on. The present paper records the observations on changes in the temperature produced by two different kinds of movements, namely gymnastic exercises and what the author calls 'mechano-therapeutic movements' such as massage, deep breathing with rolling of arms, &c.

The temperature was measured by means of a bolometer, the resistance coil being introduced into the rectum and remaining there throughout the period of observation. It was connected with the galvanometer by means of a long wire, so that the free movement of the subject was not interfered with.

Gymnastic exercises produce a distinct rise of the temperature (0·1–0·7° C.) which returns rapidly to the normal when the subject rests. The mechano-therapeutic exercises have a remarkably slight effect on the temperature, which showed a maximal rise of only 0·07° C. W. C.

Vincent, S., and Arnason, J. S. The relationship between thyroid and parathyroids. *Endocrinology*, 1920, **4**, 199.

This paper is, as the authors state, 'in the nature of a recantation'. In former papers Swale Vincent and his collaborators had expressed the view, based on experiments on cats and dogs, that the parathyroids were embryonic thyroid glands and developed into thyroid tissue when the thyroid gland was removed. Most other workers have looked upon the parathyroids as organs *sui generis*. As the result of a repetition of their experiments on rabbits the authors find that in rabbits, at any rate, the parathyroids do not develop into thyroid tissue after removal of the thyroid gland. They are therefore inclined to abandon their former point of view. There is now a general agreement that the thyroid and parathyroids are functionally distinct. W. C.

Beck, H. G. Hypophyseal disorders, with special reference to Froelich's syndrome. (Dystrophia, adiposo-genitalis.) *Endocrinology*, 1920, **4**, 185.

A useful summary with bibliography of the present state of our knowledge of the effects produced by deficiency of the function of the pituitary body. Clinical and experimental evidence is taken into consideration. The deficiency syndromes for the two parts of the gland are given as follows:—

Anterior lobe deficiency.

(1) Disturbance of growth (infantilism).
(2) Development of obesity (dystrophia adiposo-genitalis).
(3) Genital hypoplasia (infantile genitalia, with frigidity, sterility and amenorrhoea).
(4) Temperature anomalies.
(5) Cachexia hypophysoprivea.

Posterior lobe deficiency.

(1) Hypotension.
(2) Increased sugar tolerance.
(3) Diminution of basal metabolism rate.
(4) Headache, vertigo, vomiting also occur.

Polyuria (*diabetes insipidus*) which was formerly attributed to posterior lobe deficiency or hypo-activity of the pars intermedia, is not included, because the work of Houssay and of Leschke indicates that polyuria is the result of a lesion, not of the pituitary itself, but of a small area at the base of the brain around the tuber cinereum.

Curiously enough the author states that polyuria is very effectively controlled by the subcutaneous administration of 1 c.c. of pituitrin, once every two days.

The treatment of hypopituitarism which consists in the administration of thyroid gland and of pituitary gland, is briefly discussed. W. C.

Hammett, F. S. Gynecomastia. *Endocrinology*, 1920, **4**, 205.

A very clear and succinct review of the literature on this interesting condition. An exhaustive bibliography is appended. Gynecomastia is a physiological enlargement of the male breast to the volume and appearance of the normal female mamma. It may be non-painful and non-inflammatory. To the touch it gives the feel of lobulation found in the female breast; it is not accompanied by pathological stigmata. It may arise at any time after the beginning of puberty or after the termination of the changes taking place at this period. It may occur as a one-sided enlargement, but is more frequently bilateral. It is apparently not hereditary. There is evidence that the gynecomastic breast produces milk, which conclusion is supported by the histological studies of Kölliker. These indicate a structural similarity of the development of the normal male mamma to the original or nulliparous breast. Finally the anomaly may or may not be accompanied by atrophy, defect or pathological condition of the genitalia. The endocrine origin of this anomaly has been rendered probable by the recent work of Steinach, Lipschütz and Sand on the internal secretion of the testis and ovary. Castrated male rats, after implantation of an ovary, develop the characteristics of a female. The mammae develop sufficiently to nourish young animals. The corresponding change towards male characters occurs in castrated female rats after implantation of a testis.

It is therefore suggested that in gynecomasts there is present in the body somewhere in addition to testes a hormone producing tissue resembling in its effects that of ovary and sufficient to cause the abnormal development of the male mamma. W. C.

Menten, Maud L. A study of the oxidase reaction with *α*-naphthol and paraphenylendiamin. *J. Med. Research*, 1919, **40**, 433.

The oxidase reaction is a phenomenon by which many colourless chemical solutions, having the power of becoming coloured by oxidation in the air, show acceleration of this property when brought into connexion with tissues (and other substances such as alkalies, &c.) with the development of coloured granules in the cells. This is variously ascribed to the presence in the tissues of oxidases, peroxidases, reductases, or oxygenases, hypothetical substances whose enzymic nature is coming to be doubted. In the present investigation an oxidase reaction similar to that obtained in tissue was reproduced in cholesterin ester in which no enzymes occur.

The writer of this communication chose a combination of *α*-naphthol and paraphenylendiamin out of the long list of substances that have been used for this reaction, and she first settled by experiment the proportion of each to be used. The granules of indophenol that were produced in the cells were first pink, then violet, then deep blue. The reaction works best with small sections of tissue; excess of tissue apparently acts as a reducing agent, the colour disappearing.

Every kind of tissue cell, except bone, was tested in the guinea-pig, frog, turtle, white rat, and human body, and every one of them gave a positive reaction of greater or less intensity, the colour varying from pink to deep blue-black. This is a demonstration of wider distribution of the reaction than any previously recorded. The chromatin and nucleolus of the nuclei of many cells were also stained blue.

Graeff's hypothesis that a parallel exists between oxidase content and functional capacity of cell was upset by the finding of a positive reaction (though with difference of intensity) in both collecting tubules and secreting tubules of the kidney and of the ureter and vas deferens, confirming the results of Fujiwara and Ikeda.

The blue indophenol granules were seen to be condensed by an adsorption process on the surface of the lipoid globules of the cells of the suprarenal, showing Brownian movement. The retardation of the reaction peculiar to the particular oxidase reagent used favoured the study of the adsorption process.

Further, the blue reaction in nerve can be intensified by previous treatment of the nerve with ether, chloroform, &c., the entire medullary sheath then becoming loaded with discrete blue-black granules, and later changing to a confluent blue-black mass. This is analogous with the changes produced in similarly anaesthetized nerves by the Macallum reagent for revealing potassium content. It is suggested that the part played by the anaesthetic substance is disturbance of equilibrium by lowering surface tension, by which the potassium salts adsorbed on the lipoid particles are displaced and appear in an ionized condition.

The deepest reaction was met with in the neutrophil and eosinophil leucocytes. Moderately large granules were produced in the small lymphocytes. In the leucocytes the granules are more intense in colour and develop more rapidly than in the lymphocytes. This difference in behaviour can be exaggerated by modification of the test. Previous investigators (e. g. Schultze, 1909) were led to regard the oxidase reaction as a probable aid in the differential diagnosis of the two forms of leukaemia.

The suggestion arose that variations in the H^+ and OH^- concentration of the cell might in part account for the variations in intensity of oxidase reaction. The effect of this factor was studied with the Sörensen glycocoll, borate, and citrate, and with the Michaelis acetate series. The results are described and shown in tables.

That other ions play a part was shown by the behaviour of the test with the addition of sodium carbonate.

The author concludes that the theory that the oxidase content is an indication of intracellular oxidation is untenable. The oxidase reaction is an adsorption phenomenon and, as Lillie postulated, is an index of the properties of intracellular surfaces.

There are seven excellent photographs demonstrating the reaction in nerves. W. W. W.

RADIOLOGY AND ELECTROLOGY

Radio-technique.

Mazérès, G. Sur le phénomène radiographique. Lois quantitatives. Nomogramme. [**The phenomena of radiography. Quantitative laws. Calculating diagram.**] *Arch. d'électric. méd. et d. physiothérap.*, 1920, **28**, 65–107.

The paper consists of two sections; the first dealing with the theory of the production of X-rays and radiographs from the standpoint of the quantitative conversion of energy, and the second with the practical considerations of the various factors which affect the exposure of a radiograph.

In the first section the subject is dealt with in three stages. First the conversion of the energy of the electric current into the kinetic energy of the electrons in the tube. Secondly, the production of X-rays by the impact of these electrons on the anticathode and the conversion of the kinetic energy into the radiant energy of these pulsations, together with the energy lost in the form of heat and light. Thirdly, the energy of the X-rays in part reduced by absorption in the radiated tissue impinges on the photographic plate, and gives rise to the photo-chemical energy of the, latent image.

Certain other factors are then dealt with: the partial absorption of the softer rays by the glass of the bulb, the air outside, and the irradiated body; the effect of the inverse square law; the necessity for a correct exposure.

In the second section of the paper after a brief resumé of the above points a formula is deduced for the time of exposure, which involves four variables, i. e. the distance of the focus to the plate, the thickness of the object, the current and the potential difference between the electrodes. It is necessary to know also a constant depending only on the bulb and the plate used, and coefficient of absorption of the part of the body irradiated. Actual values of these constants are given for some typical cases.

To avoid the long calculation involved Dr. Mazérès has designed a form of calculating diagram with four scales corresponding to the four variables. From this diagram the time of correct exposure may be read directly.

In conclusion, the various other methods in use for determining the time of exposure are briefly described. B. D. W.

COOLIDGE, W. D. Oil-immersed X-ray generating outfits. *Am. J. Roentgenol.*, 1920, **7**, 181.

Describes a small experimental X-ray outfit, weighing 75 lb., in which the tube is mounted inside the transformer tank and in the same oil as the transformer. The tube used was a self-rectifying Coolidge tube 6 in. in length and 2 in. in diameter. Except for a small transparent window of lime glass, the tube is made of heavy lead glass $\frac{1}{4}$ in. in thickness, giving protection equivalent to $\frac{1}{16}$ in. thickness of lead. Output was 10 milliamperes at 60,000 volts. A slightly larger model had a water-cooled target and could pass 40 milliamperes at the same voltage. In this case the metal-containing tank and target were earth connected.

The chief advantages claimed for the oil-immersed system are the following:

(*a*) Eliminates all danger of electric shock to patient or operator.

(*b*) Eliminates all corona discharges with the attendant noise and odour.

(*c*) Makes it easy to obtain any desired amount of X-ray protection.

(*d*) Makes it possible to bring focal spot much nearer to patient than is ordinarily practicable. F. L. H.

CHAOUL. Das Messen in der Röntgentiefentherapie. [**Measurements in deep radiotherapy.**] *München. med. Wchnschr.*, 1919, **66**, 1475. (*J. de radiol. et d'électrol.*, 1920, **4**, 38.)

The author tested various dosimeters such as the Holzknecht, the Sabouraud Noiré, the Bordier, the Kienböck, and admits their value for the purpose of irradiation of moderate intensity, but not for the penetrating rays of deep therapy. All these indicators absorb hard rays in a totally different manner from the tissues. As Friedrich has shown, with rays of increasing hardness absorption diminishes much more rapidly in these indicators than in biological reagents. Equally unreliable are measuring apparatus founded on ionization which were introduced later. In point of fact they emit behind their aluminium screen, secondary rays, which by ionizing the air themselves, vitiate the results. According to Chaoul, the uncertainty of all these apparatus explains the diversity in the results of deep radiotherapy. It is partly because of this insufficiency that the 'erythema dose' has been adopted in the technique of deep radiotherapy. This, however, is no more satisfactory as a means of measuring because erythema is a function of regional sensibility. More rigorous still would be what one might call the maximal cutaneous dose, that is to say, the maximum dose that the skin can bear without being permanently injured. But however used as a standard cutaneous reactions only indicate quantities absorbed by the skin, never those which penetrate more deeply. The only method of arriving at a rigorous dosimeter is the systematic use of the Coolidge type of tube, excited by a transformer with closed magnetic circuit. The rays being emitted under a high voltage, and filtered by a determinate filter which only permits the shortest lengths of wave to pass, it will be sufficient to work under a given set of conditions, in order to obtain a penetrating beam, whose coefficient of absorption will always be the same. Under these conditions the biological reactions will always be identical and governed by the intensity, the time, and the distance. Finally, the deep dose for a given depth will always be a fixed fraction of the superficial dose. The author shows that with 210 kilowatts and a zinc filter 0·7 mm. thick a very hard cone is obtained, suitable for deep therapy, of which the fraction absorbed per cm. of water is 14·3 per cent. With the help of these constants it is easy to measure the extreme dose and to recognize simultaneously the dose administered to the deep tissues. This method is more precise than all those formerly used. It is self-evident that it is not of the same value if the excitation of the tube is effected by coil and interrupter. S. U. L-B.

Radio-diagnosis.

Dufour, P., et P. Étude de l'influence de la pneumatose du gros intestin sur l'image radioscopique de l'estomac. [**Influence of pneumatosis of the large intestine on the radioscopic image of the stomach.**] *Arch. d'électric. méd. et de physiothérap.*, 1919, **27**, 225. (*J. de radiol. et d'électrol.*, 1919, **3**, 523.)

A man, without pathological history, showed, when screened, a stomach forced back under the liver, to which it appeared to adhere, and further, the stomach showed a very clear biloculation in its upper half. This appearance occurred without any other explanation than considerable pneumatosis of the large intestine. In fact, on re-examination, when the pneumatosis had disappeared, the stomach had returned to its position and showed no biloculation. Considerable pneumatosis, therefore, as has been stated by several authors, can cause a false biloculation. On the other hand, the present authors have found that on insufflating the rectum, a moderate pneumatosis produces a series of notches of the large curvature similar to those observed in cases of ulcer of the small curvature. The fact that the image is inconstant cannot determine the diagnosis, for even in cases of ulcer, there are periods of inaction during which the notches disappear. One must find out if there is, either over the stomach or the duodenum, a definite painful area where pressure produces or exaggerates the notches. If the picture is inconstant, if the notches do not reappear when pressure is exerted on a painful area, it is because the anomalous gastric appearance is produced by the inequalities of a distended colon. S. U. L.-B.

Delitala. Anatomie normale et pathologique du squelette du pied au point de vue de ses lésions traumatiques. [**Normal and pathological anatomy of the skeleton of the foot, from the point of view of traumatic lesions.**] *La chirurgia degli organi de movimento,* 1917, **1**, 95. (*J. de radiol. et d'électrol.*, 1920, **4**, 89.)

From personal research on the cadaver and on radiograms collected for fifteen years at the Rizzoli Institute the author tries to throw light on the following points:

(1) The best positions for radiological examination of the skeleton of the foot.

(2) The normal relationship between the different bones, more especially between the astragalus and the calcaneum.

(3) The shape, number, and frequency of supernumerary bones of the tarsus.

(4) The radiographic criteria for a differential diagnosis between the morbid processes entailing atrophy or osseous destruction, and the neoplasms strictly so called.

(5) The radiographic criteria for a diagnosis of old and recent fractures, more especially in bone injuries due to war wounds.

It is necessary to use a constant technique if one would obtain images in which the anatomical relationships shall be constant. The author recommends the dorso-plantar position (the opening of the compressor-tube parallel to the axis of the skeleton of the foot) and the externo-lateral position (outside edge of the foot on the plate, the sole and the compressor-tube being strictly perpendicular to the sensitized surface).

On normal radiograms obtained in this way it is possible to fix constant points of pseudo-atrophy, which should be known, so that they be not confused with areas of true destructive injuries. The supernumerary bones of the tarsus have special characteristics which enable one to differentiate them from fractures of the astragalus and calcaneum; nevertheless, in certain cases it is extremely difficult to distinguish between the os trigone and a fracture-dislocation of the posterior apophysis of the astragalus.

Tuberculosis, according as it assumes a synovial or an osseous form, gives rise to a generalized atrophy or simply to a limited destructive lesion. Its commonest situations are found about the calcaneum and astragalus. Radiography has often revealed the existence there of foci the size of a pea, in a spongy bone. There are clearly defined differences between neoplastic, osteomyelitic, and tuberculous forms.

Tuberculous lesions of the scaphoid are quite distinct from those due to Köhler's disease. Fractures of the bones of the tarsus may be classified according to their radiological characters. Some are very easily recognizable, while others (longitudinal fractures of the astragalus and calcaneum, incompletely consolidated fractures) very often escape the most minute investigation. One of the pathognomonic characteristics of fractures of the calcaneum is the presence of unusual shadows which are superposed on the normal structure of the calcaneum. This is due to enclosing of dense cortical bone in the centre of the spongy substance and to the large amount of callus thrown out.

S. U. L.-B.

Radiotherapy.

Blume, P. Om Röntgenbehandling af Sarkomer. [**The X-ray treatment of sarcoma.**] *Ugesk. f. Læger.*, 1920, **82**, 943–50.

In the period 1914–1918, Blume has treated 35 cases of sarcoma at Nordentoft's Klinik. In 7 the disease proved refractory. All the remaining

28 responded immediately to treatment, and in most cases the tumour disappeared completely. But 14 patients had subsequently died, 12 from sarcoma. Only 2 of these 12 had been symptom-free for more than a year after treatment. One patient was still alive but showed signs of recurrence of the disease. The remaining 13 patients, i. e. 37·1 per cent. of the total were still alive and symptom-free 18 months to 5 years after treatment, and 12 had been symptom-free for more than 2 years. Discussing the alternatives of combined operation plus X-ray treatment, and X-ray treatment alone, B. hesitates to dogmatize over his comparatively small figures, but he notes as significant that the prognosis in his cases appeared to be almost equally good in either case, the proportion of recoveries for the combined treatment being 63·5 per cent., and for X-ray treatment alone, 60 per cent. On the other hand, the presence of metastases at the time of treatment affected the ultimate results appreciably. In 9 of 18 cases without metastases, the patients were still alive and symptom-free, whereas this was the case with only 4 out of 17 exhibiting metastases at the time of treatment. C. L.

Radium Therapy.

Schmiegelow, E. Nogle erfaringer om radiums indvirkning paa inoperable maligne nydannelseri mund- svælg- og næsehulen. [**Radium in inoperable malignant disease of the mouth, throat, and nose.**] *Hosp.-Tid.*, 1920, **63**, 50-6.

Schmiegelow began to treat malignant disease with radium in 1915, but at first the results were disappointing, probably because he used too little radium, and his technique was imperfect. Since 1917 he has obtained much better results owing to the adoption of Berven's prosthesis technique, the capsules of radium being fitted into Stent's plastic moulds which enable the radium to be kept in close contact with the diseased tissues. S. has found the difficulties of fitting the prostheses to different parts of the nasopharynx considerable; they increase the further back the disease is situated. When the new growth is situated in the sinus pyriformis or the back of the tongue, the prosthesis must first be moulded so as to fit the two backmost teeth of the upper jaw on the affected side. The prosthesis is then softened again, and its posterior part is moulded into a prolongation which extends towards the sinus pyriformis and holds the radium capsules. Such a prosthesis provokes severe irritation and salivation when there is deep-seated malignant disease of the pharynx, but if scopolamin bromide and morphin are injected the prosthesis can be retained for 24 hours without disturbing the patient's sleep.

After discussing the best means for applying radium according to the distribution of the disease in different parts of the nose and throat, S. gives details of the 13 patients he has treated in the past 2 years. One was a farmer, aged 46, with an epithelioma involving the whole thickness of the palate. Radium (20 mg. in the mouth, 10 mg. in the nose for 18 hours) was applied on four occasions at intervals of 1 to 2 months, and though the new growth had ulcerated through the palate, it disappeared completely, and the recovery was maintained when the patient was re-examined 2 years later. The results in some cases were in doubt. Thus a woman of 49, with an epithelioma of the right tonsil was treated by a combination of operation with radium. She died about 1½ years later of abdominal disease (metastases in the liver?), but there was no sign of local recurrence of the disease. One of the most striking cases was that of a man, aged 72, with a large, bleeding and ulcerating sarcoma of the nasopharynx, and considerable involvement of the submaxillary glands. These were given X-ray treatment. Three weeks after a radium exposure (30 mg. for 24 hours) he died of sepsis following an infection of one thigh. The necropsy, and a careful microscopic examination, showed complete disappearance of the round-celled sarcoma, which was replaced by healthy connective tissue. S. does not commit himself to a verdict on the rival claims of radium and the X-rays, but he is evidently much impressed by the efficacy of the former in even deep-seated malignant disease.

C. L.

Electrology.

Zimmern, A. Les méfaits de la basse tension. [**The ill effects of low tension.**] *Presse méd.*, 1920, Jan., 25. (*J. de radiol. et d'électrol.*, 1920, **4**, 141.)

In the event of contact with live wires there is no simple relation between the degree of electrical tension and the seriousness of the accident. Under certain conditions, high tension currents are not necessarily dangerous, while currents of low voltage may be so. It is possible to be electrocuted at 110 volts and even less. The danger is the same whether the subject be in circuit owing to contact with two wires, or whether he only touch one wire, thus ‘ making an earth’ owing to his good contact with the ground.

Hence, the ground should be prepared so as to protect the workman in the factory or the individual in the private house by a dry floor or a thick carpet.

The danger is intimately connected with conductivity or the intensity of the current which passes through the organism. The author speaks of a number of accidents which have happened or might happen. From the physiological point of view there is a universal tendency to accept the formula: ‘ The danger is to the heart ’. The danger will be more or less considerable, according as the lines of force cross the heart at a greater or less density. The most dangerous tract is between the left upper and lower limbs, and it is the same if the current travel from arm to arm.

From observations and statistics the alternating current is more dangerous than the continuous. There is no information concerning the maximum intensity that the human heart can stand. Different factors may modify its vulnerability. Also the fatal accidents in Germany following ‘ torpedoing ’ by the alternating sinusoidal current have been attributed to the particular sensibility of the subject, to fear, and to the effect of surprise, since the relatively moderate intensities used do not justify a fatal result.

S. U. L-B.

Electro-diagnosis.

Baudouin, G., and **Lantuéjoul, P.** Les troubles moteurs dans le zona. [**Motor disorders in herpes zoster.**] *Gaz. d. Hôp.*, 1919, **82**, 1293. (*J. de radiol. et d'électrol.*, 1920, **4**, 94.)

In 1879 Hardy pointed out that sometimes phenomena of paralysis are observed after an eruption of herpes zoster. Since then several authors have reported cases of zosterian paralysis. Be that as it may, motor troubles are rare complications, and, when they supervene, the part affected is generally the face, neck, or the upper limb. In intercostal zona, however frequent, no motor complications have been observed. Paralysis generally begins insidiously, is confined to one side, and that the same side as the zona, and is never followed by contracture. It depends upon the nerve-roots affected. Sensory, reflex and trophic disorders have been observed at the same time. Finally, there are disturbances of the electric reactions, which may be construed by total or partial R. D., or by hypo-excitability with normal qualitative reactions. The motor disturbances generally appear some days after the eruption. Paralysis may last several days, weeks, or even months, but usually disappears without leaving any ill effects. The authors consider the different clinical types according to the seat of the motor disorder; facial paralysis, paralysis of the upper limb. One case only was recorded by Hardy, of paralysis of the lower limb in the region supplied by the sciatic nerve. The fact that no case of motor disorder has been recorded along with intercostal herpes zoster seems to be explained by the clinical impossibility of diagnosing a localized paralysis in this region. S. U. L-B.

Electro-therapy

Luys, G. L'électrocoagulation en chirurgie urinaire. [**Electro-coagulation in urinary surgery.**] *Soc. de Chir. d. Par.*, 1919, May–June, 203. (*J. de radiol. et d'électrol.*, 1920, **4**, 95.)

The author employs Arsonval's bi-polar diathermy apparatus. The indifferent electrode consists of a large uncovered metallic plate of 25 × 30 cm., and the active electrode of an insulated copper wire 18 to 20 cm. long, bent at right angles and carried upon a gutta-percha handle. For treatment of the mucous membrane of the urinary passages with high frequency currents it is preferable to apply the electrode directly to the mucous membrane without interposition of liquid. The best method of application is to use the direct vision cystoscope or urethroscope. Two different actions may be obtained according as the electrode is inserted into the neoplasm to be destroyed, or is held at a certain distance from it: in the first case one obtains a deep action by electro-coagulation which destroys a large portion of the tumour; in the second case the surface is acted upon by sparking. The accidents observed after electro-coagulation are: retention of urine owing to contraction of the sphincter of the bladder, which generally passes off in about 24 hours; haemorrhage, which supervenes when the eschar separates, i. e. from 4–8 days after the operation, and ceases usually in 24 hours if a sound be tied in; infection, which supervenes on prostatic tunnelling and is a function of the urinary condition.

Electro-coagulation in the bladder. This is the best procedure to adopt in cases of vesical papilloma: several séances, generally three, at intervals of from 8 to 10 days, are necessary. In malignant disease of the bladder, high frequency currents appear to be simply palliative. Electro-coagulation in the prostate can be directed to two ends, i. e. haemostatic action for tunnelling of the prostate, or direct destruction of the hypertrophied prostatic lobes. Electro-coagulation in the urethra, and especially in the posterior urethra, has been very little used up to the present; the best instrument is the simple air urethroscope. The results obtained in papillomatous lesions are marvellous; in the penile urethra high frequency currents are very rarely employed. S. U. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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REVIEWS

TYPHOID AND PARATYPHOID

Epidemiology. The eighth annual report published by the *Journal of the American Medical Association* on typhoid in the sixty cities in the United States with a population of more than 100,000 shows an unusually large percentage of typhoid reduction, which is to be attributed partly to the immunization in the army camps of a large proportion of the particularly susceptible age group, and partly to the continued safeguarding of water and milk supplies, which have reduced the disease to so low a point that health authorities are able to devote more attention to the prevention of contact and carrier cases. The typhoid death-rate for the whole group of sixty cities is now less than 5 per 1,000.

According to Harris, director of the New York Bureau of Preventable Diseases, the death-rate from typhoid fever in New York City in 1898 was 21 per 100,000 persons in a population of 3¼ millions. The number of deaths reported was 676, and the number of deaths reported from typhoid fever during the ensuing ten years ranged from 676 to 740. Even in 1902 21 out of every 100,000 persons in New York City died of typhoid fever. In 1918, with a population of over 5¾ millions, there were only 196 deaths from typhoid fever, or 3 per 100,000. There were 2,200 cases of typhoid fever reported in 1898, and the number of cases reported in the intervening years varied in proportion to the increase in population till 1907, when 4,426 cases were reported. Since 1907, owing to the progress of sanitary science, there has been a very signal reduction of the incidence of typhoid fever in New York, so that in 1918 there was a total of only 1,238 cases although the population had increased to nearly six millions.

Aetiology. Schuman-Leclercq states that in a central hospital for enteric carriers at Vienna it was the custom to examine the bile as well as the urine and faeces before deciding that an enteric patient was free from infection. A breakfast consisting of the yolk of an egg, two biscuits, 25 grm. of butter, 0·5 grm. of Witte's peptone, and 200 grm. of bouillon was given, and two hours later the bile was withdrawn by a duodenal sound. Of 45 cases which were examined, in 17 the stools and bile were both positive, in 11 the stools were positive and the bile negative, in 4 the stools were negative and the bile positive, and in 13 the stools, bile, and urine were all negative. The writer concludes that in determining a patient's freedom from infection after typhoid, not only the stools and urine, but also the duodenal contents should be examined.

Stradiotti, of Lodi, attaches considerable importance to heredity in the incidence of typhoid fever. This relationship was first suggested to him nine years ago by an epidemic in which there were five cases in one family and seven in another, while all the other families in the commune escaped.

All the cases were severe, and three of the twelve were fatal. Since then he has often had a similar experience, so that he has become convinced that many families have a special hereditary predisposition to typhoid fever. He therefore recommends that in families in which a case occurs, especially when there is an hereditary tendency to the disease, all the other members who have not had an attack should be inoculated.

Apert and Cambessédès report an outbreak of typhoid fever in a family of refugees, seven members of which were affected, viz. the mother, her sister, and five children aged from 4 to 14. Contrary to the general rule, the epidemic was not due to drinking contaminated water, but was probably caused by direct contagion, the washing being done in the kitchen, which also served as a dining-room.

Symptomatology. Crespin and Saracino, of Algiers, maintain that typhoid fever is by no means exceptional *in the infant.* Many cases which at first sight appear to be examples of ordinary gastro-enteritis prove to be typhoid fever on more careful examination. From January 1915 to January 1918 the writers observed 42 cases in infants, 36 of which were typhoid and 6 paratyphoid. With two exceptions, in which the mothers were suffering from the disease and nursing their children (vide *Medical Science* 1920, **2**, 4), all the patients had been artificially fed, so that they had probably been infected by drinking water. In only 18 cases had the previous health been good, most of the rest being atrophic, rickety, tuberculous, or syphilitic. Most of the cases occurred in the summer or autumn, especially during the month of September. As regards the age of the patient, the younger the child the less likely it was to be attacked. Only one case occurred at the age of two months, and another at three months; between three and twelve months there were six cases of typhoid and one of paratyphoid A. The symptomatology as a rule was very incomplete. Usually digestive disturbances first attracted attention, the clinical picture being that of an ordinary gastro-enteritis. The mode of onset in most cases was indefinite. The duration of the disease was usually fairly short, not exceeding 20 to 30 days as a rule. The temperature generally fell by lysis. Convalescence was often protracted owing to persistent digestive disturbances, anorexia and loss of flesh. Rose spots were uncommon, being found in only six cases, five of which were typhoid and one paratyphoid B. The pulse was usually quick and corresponded to the temperature, the dissociation between the two which is characteristic of the disease in the adult being hardly ever observed in the infant. Enlargement of the spleen was of less diagnostic value at Algiers than in temperate climates, owing to the frequency of malaria in infants. More or less intense nervous disturbances, in some amounting to meningeal syndrome, were observed in twelve cases. Death occurred in 6 out of 36 cases, or in about 16 per cent.

Mondolfo adopts the following classification of the *atypical forms* of typhoid fever. (*a*) Anomalies in the onset of the disease, such as sudden onset, early haemorrhagic syndrome, and war typhoid. (*b*) Cases characterized by the predominance of some symptom or group of symptoms in one organ or system, while the other symptoms of typhoid fever remain latent, e. g. laryngo-typhoid, broncho-typhoid, pneumo-typhoid, pleuro-typhoid, appendiculo-typhoid, early typhoid cholecystitis, nephro-typhoid, meningo-typhoid, and early typhoid psychoses. (*c*) Anomalies in the temperature, such as rapid rise, inverted type, intermittent type, and sudden defervescence. (*d*) Larval forms which include apyrexial typhoid and ambulatory typhoid.

In cases with a sudden onset the serum test is usually positive from the beginning of the disease, whereas in ordinary typhoid it is usually negative at this stage. The early haemorrhagic syndrome is characterized by profuse epistaxis, haemorrhages from the mouth, intestine, kidneys, lungs, and uterus, and is accompanied by a state of profound prostration. In some cases, however, the haemorrhages may be confined almost entirely to the skin. Frugoni has described two special forms of war typhoid, namely, a bronchitic form characterized by intense diffuse bronchitis and a rheumatic form with sudden onset, high fever, and diffuse pains in the joints and muscles. Three forms of pneumo-typhoid are described by Mondolfo. In the first pneumonia dominates the clinical picture at first; subsequently the characteristic symptoms of typhoid appear, and the respiratory symptoms subside. In the second form the symptoms of pneumonia and typhoid coexist from the onset. In the third form the disease is dominated by the signs of pneumonia and the typhoid symptoms pass almost unnoticed. Appendiculo-typhoid is a variety of the disease which commences with symptoms of appendicitis, while the ordinary symptoms of typhoid are latent. In such cases the following signs are in favour of typhoid as against appendicitis: indefinite localization of the pain in the right iliac fossa, absence of rigidity of the abdominal wall, a comparatively slow pulse in relation to the temperature, headache, stupor, albuminuria, and an enlarged spleen. The pain which in appendicitis is spontaneous and most intense at McBurney's point is more diffuse and less severe. Lastly, leucopenia is in favour of typhoid, while leucocytosis indicates appendicitis, though in exceptional cases appendicitis may not be accompanied by leucocytosis. The term 'apyrexial typhoid' is used for cases in which no rise of temperature has been observed throughout the disease, or in which fever has been absent during a certain time or was so slight as barely to reach a sub-febrile level. The other symptoms may appear and succeed one another as in ordinary typhoid so that apyrexia is the only atypical part of the syndrome. Sometimes the fever lasts only for a very brief initial period, and the disease is subsequently apyrexial. The cause of apyrexial typhoid is not known. The hypothesis of an attenuated infection may be excluded, or at least it does not explain the severe or fatal cases. The view which appears to be supported by experimental and clinical evidence is that the apyrexia depends in some cases on the gravity of the infection. Thus in Rodano's case the apyrexial period coincided with an aggravation of the disease which ended fatally. Experimentally it has been shown that, while moderate doses of the typhoid bacillus cause a rise of temperature, higher doses produce hypothermia.

Under the name of protracted *colo-typhoid*, von Lippmann, of Frankfort, describes five fatal cases which presented the following characteristics. After the temperature had become normal, the patient showed no tendency to recovery, but had a persistent diarrhoea differing from dysenteric stools in the absence of blood, mucus, and pus. Progressive emaciation set in, and finally cachexia accompanied by oedema and marantic skin haemorrhages. On post-mortem examination typhoid ulcers were found in the large intestine from the ascending colon to the rectum. Bacteriological examination showed that the condition might be due to typhoid or paratyphoid A.

Typhoid fever in the inoculated. In a paper on typhoid fever in the American Expeditionary Force, based on the study of 370 cases, Vaughan comes to the conclusion that the clinical picture of typhoid in those who had been given the triple typhoid vaccine was similar to that in the unvaccinated, absence of leucocytosis, continued fever of the usual course and duration, rose spots, palpable spleen, relapses, and complications remaining the characteristic features of the disease. The mortality in the series was 11 per cent. The percentage of positive results from cultures of the blood, urine, and faeces, and the duration of the bacteriaemia were almost the same as in non-vaccinated patients. The average severity of cases infected within eight months after vaccination was less than 10 per cent. After eight months the severity percentage gradually increased. The onset of the disease was more frequently acute when occurring within the first month after inoculation. In 16 cases with an onset from seven to twelve days after inoculation (the usual incubation period) the infection probably occurred during the interval after inoculation. Paratyphoid infections though much milder as a group, could not be distinguished clinically from typhoid fever and were of much less frequent occurrence. Vaughan thinks it probable that a large number of vaccinated persons were infected with typhoid or paratyphoid but never become sufficiently ill to be admitted to hospital.

Typhoid and tuberculosis. From observations on 11 patients with pulmonary tuberculosis who contracted typhoid fever in a sanatorium, Clovis and Mills come to the following conclusions: (1) Patients with inactive pulmonary tuberculosis may have typhoid fever without any detrimental effects on the pulmonary condition, while the general condition may often be benefited. (2) Patients with acute pulmonary tuberculosis may have typhoid fever and recover without a more rapid advance in the pulmonary condition than would have occurred had they not had typhoid. (3) Pulmonary tuberculosis does not appear to have any effect on the course of typhoid fever. (4) A high caloric diet is advisable during the height of the disease, and prolonged rest in bed in convalescence should be ordered as a precautionary measure. (5) Prophylactic injections of typhoid vaccine, which were given to 62 tuberculosis patients, caused severe reactions only in the active cases, but had no permanent bad effects.

Typhoid and malaria. Scott, Government bacteriologist in Jamaica, who records 11 illustrative cases, states that though enteric fever in Jamaica is a severe affection with a comparatively high mortality, and malarial infection in Jamaica is also a severe condition, in most cases being of the subtertian variety, coincident enteric fever and malaria in many instances at least is remarkably mild in type and in course, and recovery is usually more rapid and complete than in the case of either affection separately (vide *Medical Science*, 1919, **1**, 263; 1920, **2**, 323–4).

Strisower reports the case of a medical man, aged 26, who had typhoid fever at 17 and nine years later contracted malaria and jaundice. Typhoid bacilli were found in the blood, the duodenal fluid, and the stools, although there was no clinical evidence of typhoid fever. Strisower suggests that the patient was a typhoid carrier in whom the bacilli were driven from the bile passages into the blood in consequence of the attack of malaria and jaundice.

Paratyphoid fever. During the epidemic of enteric fever at Jassy in 1917–18, Nitzesco had under his care three cases of typhoid associated with paratyphoid infection. In the first case typhoid was immediately followed by paratyphoid A which proved fatal, death being due to intense adynamia. *Post mortem* the intestine showed numerous characteristic ulcers in Peyer's patches, and cultures from the blood, spleen, and intestine showed the paratyphoid B bacillus. The second case was an example of typhoid fever with an area of pulmonary congestion due to the paratyphoid B bacillus, and subsequently complicated by sero-purulent pleurisy. In the third case typhoid fever was complicated by sero-purulent pleurisy due to the paratyphoid B bacillus. Nitzesco thinks that if investigations were made in all cases of pleuro-pulmonary complications in typhoid, as well as repeated blood-cultures, examples of mixed infection would be found to be more numerous.

According to Vallardi, director of the bacteriological department of the Italian Expeditionary Force, *paratyphoid A* was very prevalent during the triennium 1916–18 in the Army of the East. In his opinion the previous diffusion of the disease in Eastern Europe was increased by the presence of French and English colonial troops, and in support of this view he alludes to statistics which show that though the French and English used T.A.B. vaccine and the Italians a vaccine against typhoid and paratyphoid B only, the incidence of paratyphoid A was higher among the French and English than among the Italians. The mortality from paratyphoid A, both among the Italians and the other Allies, was much less than that from typhoid or paratyphoid B, and ranged from 0·84 to 3·03 per cent. Vallardi found numerous paratyphoid A carriers in the Italian Expeditionary Force in individuals with intestinal syndromes due to various causes such as acute or chronic bacillary or amoebic dysentery.

Federschmidt reports a local outbreak in Nuremberg of 65 cases of severe gastro-enteritis following the consumption of sausages composed of horse-flesh, examination of which showed the presence of *paratyphoid B* bacilli. The onset of the symptoms occurred a few hours after taking the food and consisted of vomiting, abdominal pain, profuse diarrhoea, and high fever. Recovery took place in three to four days. It was a remarkable fact that all the patients agreed that the sausages did not have a bad smell or taste. Examination of the stools immediately after recovery and eight days later did not show any paratyphoid B bacilli.

Schmid describes an epidemic of ten cases of paratyphoid B in a lunatic asylum in which a carrier who had probably been infected by some article of food was the source of infection, the other cases being due to contact infection. As all the cases occurred in the section for maniacal women, and the most restless or demented patients were chiefly attacked, a complete examination was impossible. As far as could be determined, the febrile period, which was accompanied by vomiting, diarrhoea, or constipation, ranged in the individual cases from eight days to four weeks.

Garrow reports a sporadic case of *paratyphoid C* fever in East Africa, in this respect differing from the cases described by Hirschfeld in the Serbian army in Macedonia, and by MacAdam and Mackie and Bowen in Mesopotamia, in both of which areas the disease appears to have been more or less prevalent if not actually epidemic. As in Hirschfeld's cases, Garrow's patient showed the cardinal signs of a moderately severe attack of enteric fever, and there were no lung signs beyond a few moist râles at the base, whereas in the cases of paratyphoid C reported by MacAdam and Mackie and Bowen the pulmonary symptoms were so prominent that a diagnosis of pneumonia was made.

Complications. Gautier and Brutsch, of the Geneva Medical Clinic, report a case of *peritonitis* following perforation of a typhoid ulcer in a man aged 26 in which an interval of a month elapsed between the occurrence of the perforation and death. At the autopsy an adhesive peritonitis was found localized in the right iliac fossa, and a sac containing faecal matter. The intestine showed multiple perforations, including one in the large intestine. The writers allude to a similar case in Dieulafoy's text-book. A striking feature in the present case was the mild character of the onset of the typhoid attack, the patient being able to continue his work for a fortnight, when perforation suddenly took place, manifested by fall of temperature, hiccough, vomiting, and constipation. The peritonitis became rapidly localized, but from time to time there was an exacerbation of the symptoms, probably due to a fresh perforation. Various haemorrhagic manifestations were observed, viz., intestinal, renal, and cutaneous haemorrhages, which were due not merely to the typhoid toxins, but also to the superadded toxaemia caused by the peritonitis and the retention of faecal matter in the peritoneum. Lastly, the patient showed a considerable loss of flesh (two-fifths of his weight) during the month which elapsed between the perforation and his death.

Arcangeli has collected 49 cases of typhoid fever which were operated on in his hospital and private practice for perforative peritonitis with a recovery rate of 38·7 per cent. 10 which were operated on within the first nine hours all recovered. Of 20 operated on within 12 hours 15 recovered; of 20 operated on between 12 and 24 hours only two recovered, and those operated on after 24 hours all died.

Reid and Montgomery, of the Surgical and Paediatric Clinics of the Johns Hopkins Hospital, have collected 18 cases of typhoid fever in children who either died from or were operated on for *acute cholecystitis*. Eight cases which occurred prior to 1893 died without operation. Since then, 10 cases which have been treated surgically have been reported with only one death. In recent years, cultures of the gall-bladder have been made at the time of the operation. When there was a pure culture of the typhoid bacillus, the leucocyte count was relatively low, about 10,000. The writers emphasize the importance of differentiating between gall-bladder complications which do and those which do not require operation. Slight pain and tenderness in the region of the gall-bladder, with slight degree of spasticity of the rectus, are not uncommon in typhoid fever, and the vast majority of such patients get well without operation.

Panayotatou, of Alexandria, reports a case of typhoid infection localized in the gall-bladder in a woman aged 24. There were no intestinal symptoms, but the typhoid bacillus was isolated in pure culture from the pus of the suppurative cholecystitis. A case of acute angiocholecystitis due to typhoid septicaemia, but without any symptoms of typhoid fever was also reported by Fiessinger to the Société médicale des hôpitaux de Paris, in a man aged 44, and in the subsequent discussion Netter related two similar cases.

Marchand describes two fatal cases of *haemoptysis* in typhoid fever, in a man aged 45 and a girl aged 17, in whom the haemorrhage was due to erosion of a vessel at the margin of a laryngeal ulcer. He also records a case of *laryngeal pneumatocele* in a boy aged 16, which subsided spontaneously and had probably been caused by escape of air during coughing, through an ulcer in the region of the vocal cords.

Laroche and Peju propose the following classification of *meningeal manifestations* in typhoid fever: (1) Meningeal syndrome with a clear cerebrospinal fluid in which the cell and albumin content is little if at all affected and the culture is negative. This form is nearly always mild, and generally clears up rapidly without any influence upon the prognosis. It is most frequent at the onset of typhoid, but may also occur at the height of the disease or during its decline. As a rule it is of short duration, but sometimes lasts several days, and in exceptional cases several weeks. (2) Meningitis in which typhoid or paratyphoid bacilli are cultivated from the cerebrospinal fluid is much rarer. The fluid is clear or turbid, but rarely purulent. The prognosis is grave, death being observed in about half the cases. The writers record an instance of this kind in a man aged 27 during a relapse of typhoid septicaemia. The symptoms were mild and transient, but the cerebrospinal fluid was turbid and contained an extremely large amount of typhoid bacilli which disappeared entirely after two lumbar punctures. Recovery was uneventful. (3) Suppurative meningitis due to secondary infection with staphylococci, pneumococci, streptococci, &c., with or without typhoid or paratyphoid bacilli. This form of meningitis is always fatal.

Baumgartner and Olsen have collected 23 cases of purulent typhoid meningitis, including a personal one in a boy aged 6, also complicated by otitis and cholecystitis, in patients aged from 4 months to 55 years. In all the cases pure cultures of the typhoid bacillus were obtained from the spinal fluid, in most instances before death, which occurred in every case. There was a frequent lack of the usual typhoid lesions, although many of the cases showed a positive Widal's reaction and blood-culture.

Pezzi and Milla illustrate the rarity of meningitis in enteric fever by stating that out of 244 cases of typhoid and 194 cases of paratyphoid A and B admitted to the Mantegna Hospital at Milan, only two cases occurred. In both instances the typhoid bacillus was found in the turbid cerebrospinal fluid. In the first case, which proved fatal, the typhoid bacillus was associated with a diplococcus which probably facilitated its invasion, and in the second case, which recovered, the invasion of the meninges was favoured by hereditary nervous taint, alcoholism, and especially by a pre-existing cerebral lesion probably of syphilitic origin.

A fatal case of *Landry's paralysis* in typhoid fever is reported by Macchi, of Milan, in a woman aged 37. The symptoms developed on the twenty-eighth day of disease, and death took place two days later. The lesions, which were not characteristic, inasmuch as they might be found in various acute infections, consisted of a very mild form of meningo-myelitis and degenerative changes in the peripheral nerves.

Estrada, of Mexico, reports six cases of *ocular complications* of typhoid fever, five of which were examples of optic atrophy, and one of iridocyclitis. In two there was a history of acquired syphilis, and two were obviously the subjects of the inherited disease. Estrada points out that the optic neuritis found in typhoid fever in no way differs from that of syphilis. In both there is an insidious onset and a slow and progressive course, ending, after a varying period of time, in complete blindness. The same is to be said of the iridocyclitis met with in both diseases. Estrada emphasizes the importance of looking for syphilis in every patient with a post-typhoid ocular complication. Even if there is no history or clinical evidence of syphilis, the Wassermann reaction in the blood and cerebrospinal fluid should be tested, or, if this is impossible, antisyphilitic treatment should be adopted. It is very probable that if patients with post-typhoid optic neuritis or irido-cyclitis become blind, it is due to their not having had such treatment or its being instituted too late.

Étienne, of Nancy, records three cases of *phlebitis* which were shown by blood-culture or Widal's reaction to be due in the first case to the typhoid bacillus, in the second to the paratyphoid A bacillus, and in the third to an undetermined paratyphoid bacillus. In none of the cases were there any other signs of enteric fever. In the case of paratyphoid A infection, phlebitis of the left femoral vein marked the onset of the disease after a prodromal febrile period of about a week. In the typhoid case phlebitis of the type of phlegmasia alba dolens developed on the third day, first on the left side and then on the right, and in the third case the disease started with phlebitis of the left lower limb followed by a rise of temperature to 100·4, occurrence of phlebitis in the right lower limb, and an attack of jaundice.

From examination of 157 cases of *paratyphoid bacteriuria,* 72 of which were due to paratyphoid A, and 85 to paratyphoid B, as well as of a large number of controls consisting of paratyphoid cases without bacteriuria, Herrnheiser found that bacteriuria was more frequent in severe than in mild cases. The average frequency was about 40 per cent. The onset of the excretion of bacilli began as a rule in the second to fourth week, but might be delayed till the seventh week. Three types of bacteriuria could be distinguished according to their duration and course: (1) an ephemeral type in which the bacilli were found in the urine for only one day, or two successive days, in spite of daily examination of the urine. (2) Continuous excretion, the organisms being found constantly for days, weeks, months, and even years. (3) Intermittent excretion, in which the urine was sterile for days or weeks at a time. Each of the types might occur both in paratyphoid A and B, but ephemeral bacteriuria appeared to be more frequent in paratyphoid B, and intermittent bacteriuria in paratyphoid A. The bacteriuria disappeared as a rule in paratyphoid B from the second to the seventh week, and in paratyphoid A from the fourth to the tenth week. From examination of the urinary sediment which showed a great increase in the number of leucocytes, from catheterization of the ureters which showed inflammatory changes in the upper part of the urinary tract, and from autopsies in which multiple small abscesses were found in the kidneys, Herrnheiser comes to the conclusion that the bacteriuria was not due to an ascending infection from the urethra or to a blood infection, but was caused by rupture of the small renal abscesses into the uriniferous tubules.

Weinberg and Françon report a case of *gas gangrene* of both thighs which occurred on the eighteenth day of a severe attack of typhoid fever. Its development was arrested by anti-gas gangrene serum, but death took place in three days. The writers could find only three other similar cases on record. In all four cases the patients had been given injections of drugs in the thigh, such as adrenalin, normal saline, spartein or tincture of musk. The writers do not think that the injection site was the portal of entry of infection, but that it merely served as a localizing point for the anaerobic organisms in the blood, the slight trauma produced providing a favourable condition for their development, like the *bistournage* in Chauveau and Arloing's classical experiment.

Rathery and Bonnard, related to the Société médicale des hôpitaux de Paris, two cases of severe typhoid fever in which *abscesses* containing the typhoid bacillus appeared in convalescence, in both instances at the site of a previous trauma (an operation scar in one case and a fixation abscess in the other). The time which elapsed between the trauma and the development of the abscess was considerable, being 21 days in the operation case and 27 days in the case of fixation abscess. In the subsequent discussion Widal also related three cases of abscesses containing typhoid bacilli which developed in convalescence from typhoid fever, in the first case at the site of injections of caffein and normal saline, in the second at the site of a tuberculous gland, and in the third in an ovarian cyst.

Damade also records a case in which typhoid bacilli were isolated from a fixation abscess in very severe typhoid fever and alludes to other instances reported by Carles and Lesieur.

In an article on rare forms of suppuration following paratyphoid, Martens reports cases of single or multiple abscesses of the liver, multiple renal abscesses and pulmonary abscess due to paratyphoid B, and a case of a large abscess in the thigh due to paratyphoid A.

Klein and Torrey, of the University of Pennsylvania, report four cases of paratyphoid fever with *pulmonary complications*, three of which were due to *B. paratyphosus* B, and one to *B. paratyphosus* A. In one case there was frank lobar pneumonia, and in the other three broncho-pneumonia. In one case *B. paratyphosus* A was recovered from the sputum. The writers conclude that there is a definite pulmonary form of paratyphoid fever which may be easily mistaken for any of the acute respiratory infections, especially as the pulmonary symptoms often precede any intestinal manifestations. In view of the findings of Minet (vide *Medical Science*, 1920, **2**, 3), who regards the paratyphoid bacillus as the aetiological factor in cases of chronic bronchitis, the writers recommend that the sputum of chronic pulmonary invalids should be examined for this group of bacillus.

Inoculation. Russell shows that antityphoid vaccination, though carried out by a staff that had not been carefully trained in its administration, gave a high degree of protection to the forces under the conditions of hurried mobilization and of warfare, and reduced the rate not only below the rates for previous wars, but also below the rate found in civil life in some of the older states where the entire population is protected by sanitary measures. Thus the army rate for 1918 was 0·03 for troops in the United States and 0·08 per thousand in the American Expeditionary Force, as compared with 0·14 per thousand among young men of corresponding age at home under peace conditions.

According to Russell, during the period of America's participation in the war (April 6, 1917–November 11, 1918), approximately 4,000,000 men served in the army, and during the full two years there were 1,065 cases of typhoid, or one among every 3,756 men, and 156 deaths, or one death among 25,641 men. In the Spanish-American war, on the other hand, there was one case for every 7 men, and one death among every 71 men.

Basten states that owing to an outbreak of typhoid fever in Euskirchen, Weilerswist, and Merten, three German towns in British occupation, with a total population of 21,248 inhabitants, compulsory inoculation of all persons from the age of 6 to 55 was ordered by the British authorities. 14,343 persons were inoculated twice with T.A.B. vaccine, with an interval of ten days between each injection, as in the case of the civilian population of Flanders during the war (vide *Medical Science*, 1919, **1**, 25–6). Those suffering from febrile diseases or advanced pulmonary tuberculosis, and women in the last three months of pregnancy and in the first three months after delivery were excused. As no bad effects on nursing were observed, inoculation was subsequently made compulsory four weeks after delivery.

It was found that the incidence of typhoid fever among the 14,343 inoculated and the 6,905 non-inoculated inhabitants was about the same, 17 cases occurring among the former and 7 among the latter. Basten attributes this to there being only two inoculations instead of three as practised in the German army, and partly to the fact that the non-inoculation of one-third of the inhabitants increased the likelihood of infection for the inoculated. On the other hand the inoculations appeared to have a favourable effect on the severity of the disease, the mortality among the inoculated being 13 per cent. as compared with 19 per cent. among the uninoculated. Another advantage of inoculation was that it caused many cases in the incubation stage to develop at once, and so enabled infected cases to be separated from the rest of the population. In Basten's opinion adequate protection against typhoid can be obtained by three injections and by inoculating all persons from 3 to 70.

In his report on antityphoid and antiparatyphoid inoculation in the Royal Navy for 1918–19, Bassett-Smith states that from October 1, 1918, to September 30, 1919, 17,401 men were inoculated, 2,273 being given one inoculation, and 15,128 two inoculations. During the year the total number of cases of enteric fever was 48, the incidence being as follows:

	Total.	Typhoid.	Para. A.	Para. B.
One inoculation	11	10	1	0
Two inoculations	10	8	1	1
No inoculations	27	24	1	2
	48	42	3	3

There were five deaths among the inoculated. Of the eight typhoid cases who had been inoculated before they contracted the disease a period of three years had elapsed in two; in the other six the interval was between 12 and 18 months. In the cases of paratyphoid A and B which had had two inoculations, the period in each was two years before the onset of the fever (cf. *Medical Science*, 1919, **1**, 29).

Galambos brings forward the following arguments against the efficacy of antityphoid inoculation: (1) In the summer of 1917 he had occasion to observe an outbreak of 33 cases of enteric fever among Austrian soldiers. Typhoid fever was diagnosed in 23 cases and paratyphoid in 10 cases. All the patients without exception had been inoculated. The great majority had enlisted in the beginning of 1917 and had been inoculated twice in April and once in June. A few had been inoculated in the previous year. In some of the cases the last inoculation in June coincided with the beginning of the incubation period. Every one of the cases presented the typical clinical picture of enteric fever, the attacks being severe on the average. Seven of the cases were fatal and the post-mortem lesions were typical of enteric fever. (2) Galambos suggests that many of the cases included in inoculation statistics were not really enteric fever at all. Thus in one isolation hospital it was stated that among several hundred cases of typhoid fever there was not a single death. Even if it be granted that inoculation was followed by a decline in the incidence of typhoid fever, this would not be a proof of the efficacy of inoculation, as a similar decline in the incidence of the disease occurred during the Franco-Prussian war in 1870–1. (3) The difference in the mortality in inoculated soldiers and the uninoculated civilian population cannot be regarded as an argument in favour of inoculation, as the mortality from dysentery in soldiers, apart from antidysenteric vaccination, is much lower than in civilians. Galambos concludes that though antityphoid inoculation in association with other factors may play an important part in reducing the incidence of typhoid fever, its influence on the mortality cannot be regarded as proven.

Foster describes certain unusual reactions to typhoid-paratyphoid vaccination which he observed among 40,000 vaccinated troops. The symptoms suggested certain specific diseases which he divides into meningeal, appendical, and purpuric types. The reaction which bore resemblance to appendicitis was the commonest. At least 50 of these cases were studied, and of the other types a somewhat smaller number. The clinical picture so closely resembled appendicitis, owing to the local pain and tenderness, slight fever, and some increase in the leucocyte count, that a number of cases were operated on, but the appendices did not present the conditions expected. In the meningeal type lumbar puncture showed the condition to be one of meningismus, but the fluid was clear and sterile, with no significant cell increase. In the purpuric type epistaxis and transient haematuria were not uncommon. Some of these cases also showed haemorrhages and purpuric rashes. Neither examination of the blood nor the history threw any light on the condition.

Diagnosis. The occasionally close resemblance of typhoid fever to typhus and the impossibility of diagnosis without laboratory assistance is illustrated by a case of typhoid fever reported by Cerrano in a boy of 13, in whom the following points were in favour of typhus: (1) the sudden onset; (2) the early appearance of nervous symptoms such as stupor, delirium, and incontinence of the urine and faeces; (3) the lack of abdominal symptoms; (4) the appearance and course of the fever; (5) the character of the pulse, which was always more frequent than is usual in typhoid, even allowing for the age of the patient; (6) the early appearance of the eruption (fourth or fifth day) and its definitely petechial character—a rare occurrence in typhoid; (7) the history, in which infection by drinking water appeared to be excluded. On the other hand the Weil-Felix reaction was negative, Widal's test was positive, and a blood culture showed typical colonies of typhoid bacilli.

Guillain, Laroche, and Libert report a case in a woman aged 19, in whom the clinical symptoms simulated those of acute polyarticular rheumatism, but a blood culture revealed the presence of typhoid septicaemia. The writers conclude that a blood culture is indispensable in febrile disorders even when the diagnosis appears certain.

According to Totta the typical form of typhoid fever is an exception at Porto Alegre in Brazil. The cases are liable to be mistaken for febrile gastric disturbance or for the gastro-intestinal form of influenza. Totta concludes that in the case of a febrile patient whose symptoms do not permit of a precise diagnosis the possibility of typhoid fever should always be considered and a blood culture and Widal's reaction employed.

Treatment. Rodet and Bonnamour, who had previously reported on 127 cases of typhoid fever treated exclusively by Rodet's serum (vide *Medical Science*, 1919, **1**, 31), now relate the results obtained in 119 more cases, or a total of 246. They found that the serum had a definite action, which was shown by pronounced changes in the temperature, and better still by a very marked diminution of toxic symptoms and a shortening of the duration of the disease. The best results were obtained when the serum was used early, but it might produce a favourable effect at all stages of the disease, if employed before the occurrence of complications It had no ill effects and no contra-indications. If used at an early stage it prevented complications and lowered the mortality. The total mortality among the 246 cases was 11 per cent., which was reduced to 8·4 per cent. if only the cases treated before the twelfth day of disease were taken into account. The higher mortality than in the first series of cases (2·9 per cent.) is attributed to the greater frequency of secondary infections due to the epidemic of influenza.

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J. D. R.

DISEASES OF DUCTLESS GLANDS

Thyroid. According to Blank, the contradictory statements in the literature as regards the diagnostic value of the blood picture in hyperthyroidism and goitre are due to difficulties of diagnosis, errors of technique, variations in the blood count in hyperthyroidism, and too narrow a conception of the normal values. Blank examined the blood in 17 cases of pure Graves's disease, 28 cases of Basedowoid, i.e. cases in which the cardinal symptom of hyperthyroidism, viz. cardiac and vascular disturbance, was present, but the other symptoms were less pronounced, and 41 cases of ordinary goitre. His results were as follows: (1) In about 30 per cent. of cases of hyperthyroidism there was poikilocytosis. (2) Typical Graves's disease is distinguished from Basedowoid and goitre by thrombopenia, which is present in 43 per cent. (3) The haemoglobin content is normal in only 28 per cent. of cases of Graves's disease. Its diminution has no diagnostic significance, but its increase is more in favour of Graves's disease than of Basedowoid. (4) Hyperthyroidism and goitre show no difference from one another as regards the number of the red cells. (5) Individual cases of Graves's disease show considerable oscillations in the colour index. (6) The leucocyte count has no value in differential diagnosis. (7) In 50 per cent. of the cases of hyperthyroidism and goitre polychromasia occurs, and basophil stippling occurs in 50 to 75 per cent.

According to Goodall, the changes which the heart undergoes in Graves's disease are as follows: (*a*) tachycardia, 120 to 200 a minute, leading to (*b*) myocardial exhaustion associated with (*c*) atonia, with relative valvular incompetence; (*d*) dilatation; (*e*) myocardial degeneration; (*f*) auricular fibrillation. As medical treatment in such cases is unavailing, X-rays or surgical removal of gland substance is indicated as the only means of reducing thyroid activity or neutralizing the secretion or its effects.

The tendency of Graves's disease to simulate tuberculosis, especially in the female sex at puberty and the menopause, is emphasized by Sergent, who points out that in such cases the clinical picture of Graves's disease may be complete or only minor signs may be present. In both pulmonary tuberculosis and hyperthyroidism the following symptoms may be found either separately or in combination, viz. an unsettled temperature, an unstable pulse usually characterized by attacks of more or less marked tachycardia, variations of the blood-pressure, irregular menstruation, flushed face, sweating, loss of flesh, fatigue, attacks of abdominal pain and diarrhoea, cough, and shortness of breath. Sergent concludes that at both extremes of the sexual life of woman the possibility of hyperthyroidism should be borne in mind, and that the presence of pulmonary tuberculosis should only be admitted if there are definite proofs of its existence.

Pfeiffer, of Dijon, records 3 cases of acute Graves's disease in which the causal emotion, which was insufficient in itself to produce a permanent anatomical change, was accompanied by an important factor, viz. active syphilitic infection. As these 3 cases were the only examples of so-called emotional exophthalmic goitre which he had met with during 18 months' observation of several hundred cases of commotion, Pfeiffer is convinced that every case of exophthalmic goitre of so-called emotional origin occurs on a syphilitic soil.

Lahey, of Boston, reports a case in a woman of loss of both eyes from the exophthalmos of hyperthyroidism, oedema and ulceration of the cornea necessitating enucleation first of the right and then of the left eye. The case had previously been treated by X-rays and removal of the superior cervical ganglion on the left side. In such cases, as Lahey points out, the best treatment would have been removal of a considerable portion of the thyroid gland.

Although as a rule acute infections occurring during the course of Graves's disease cause a marked increase in the severity of all the symptoms, in some cases such infections apparently injure the gland to such an extent as to result in eventual alleviation of the condition. Squier reports two cases of hyperthyroidism in which complicating infections (tonsillitis in one case and rhinitis, otitis, and mastoiditis in the other) caused a marked increase in the severity of the thyroid symptoms, followed, after the acute infection had subsided, by striking improvement, if not cure. Squier suggests that the improvement was due to actual loss of secretory tissue through post-infective sclerosis of the gland.

Rachford reports the case of a woman, aged 64, suffering from goitre with symptoms of hyperthyroidism. The enlargement above the sternum was very marked, and the tumour also extended below the sternum, and by pressure on the right phrenic nerve produced paralysis of the right side of the diaphragm, and by pressure on the recurrent laryngeal nerve caused partial paralysis of the right vocal cord; it also displaced the heart to the right side, producing a loud systolic murmur, most intense at the apex, and marked myocardial insufficiency. Under treatment with rest, X-rays, and medication, she made a fairly satisfactory recovery, but paralysis of the diaphragm and vocal cord persisted.

Peabody, Sturgis, Tompkins, and Wearn state that epinephrin hypersensitiveness, as indicated by the positive reaction after epinephrin injections according to Goetsch's method, had become so generally regarded as of specific diagnostic significance in hyperthyroidism that they determined to study the conditions under which it might occur. In normal individuals it was not present in a group of 26 seasoned soldiers; it was present in 14 per cent. of 28 medical students, and in 48 per cent. of 103 soldiers without evidence of organic disease but with the symptom complex of the effort syndrome. 7 psychoneurotics all gave positive results. Among hospital patients 17 per cent. of 17 patients with organic heart disease and 57 per cent. of 21 patients convalescent from acute infections gave positive reactions. Positive reactions were found in only 15 out of 21 cases of hyperthyroidism; 6 unquestionable cases with within 21 and 35 per cent. above normal gave negative reactions. Owing to the wide distribution of the reaction among persons in whom there was no evidence of hyperthyroidism, the writers conclude that the test does not possess any specific significance in the diagnosis of that condition.

Woodbury made comparative observations with Goetsch's test and the determination of basal metabolism advocated by Benedict, Du Bois, and others (vide *Medical Science*, 1920, **2**, 126–7), and found that the epinephrin chloride test was more sensitive and required even greater safeguards than the estimation of oxygen consumption. He concludes that complete methods of examination with special attention to the possibility of errors in cases of psychoneurotic patients should furnish the basis for diagnosis rather than reliance on any functional test, though functional tests are of great value in compilation of evidence, especially in relation to the degree of toxicity.

The importance of removing any possible source of bacterial toxaemia, on which Meredith insists, in the treatment of early hyperthyroidism is illustrated by Barber, who records a case of urticaria of 8 years' duration in a girl of 21, associated with hyperthyroidism. The condition was attributed to chronic toxaemia, probably of streptococcal origin, as a complete cure followed removal of infected tonsils.

In a paper on the non-operative treatment of Graves's disease Klewitz, of the Königsberg University Medical Clinic, first enumerates the cases which are not suited for such treatment, viz.: (1) Cases in which there is a suspicion of malignant degeneration as shown by rapid growth and hardening of the goitre, difficulty in swallowing, pain in the cervical plexus, paralysis of the recurrent laryngeal and sympathetic, and increasing cachexia. (2) Cases with definite symptoms of compression of the trachea or oesophagus. (3) Cases of colloid or cystic goitre. (4) Chronic cases generally. There is no absolute rule in such cases, but, generally speaking, cases which have lasted longer than 5 years are unsuited for medical treatment. On the other hand, the cases which are suitable for medical treatment are the *formes frustes*, and the acute and subacute cases. Klewitz regards the criteria of successful treatment to be improvement of the nervous symptoms, diminished frequency of the pulse, increase of body weight, and, most of all, ability to return to work. The exophthalmos and thyroid enlargement do not always subside even when the treatment is successful.

The frequency of gastro-intestinal symptoms in disturbances of the thyroid is emphasized by Kohn, who, in examination of the histories of 111

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Lines 19, 27, 40, 46, *for* 'hyperthyroidism' *read* 'hypothyroidism'

cases of thyroid disease treated in the Surgical Service of the Johns Hopkins Hospital, found a past history of gastro-intestinal disturbance in 61 instances and a present history of gastro-intestinal disturbance in the same number of cases. Kohn, therefore, insists on the importance of excluding thyroid disease in cases with gastro-intestinal disturbance.

Escudero states that disturbance of the function of the thyroid may give rise to gastro-intestinal symptoms which may be grouped under the name of thyroid dyspepsia. Clinically two forms may be described, viz. those corresponding to thyroid insufficiency and those caused by hyperthyroidism. The first group is characterized by a tendency to low gastric values, and the majority of cases of hypochylia and achylia belong to this group. The second group shows a tendency to high gastric values, but the sensory disturbances are the first to appear and persist. Disturbances of secretion may be absent and may vary from heterochylia to permanent gastric hypersecretion. Chronic gastritis is the necessary termination of these cases if they do not clear up spontaneously or are not cured by suitable treatment, viz. thyroid opotherapy for insufficiency and antithyroid treatment for hyperthyroidism.

Constipation as one of the manifestations of hyperthyroidism is discussed by S. G. Strauss, who recommends doses of gr. $\frac{1}{10}$ thyroid extract given on an empty stomach either first thing in the morning or at bedtime. The dose is given once a day for a week and the result noted. If it has no effect after a week's administration it should be increased to $\frac{1}{2}$ gr., then to 1 gr., and so on. As soon as the intestinal function is normal the thyroid extract should be stopped.

Hinz, of the University Medical Polyclinic at Rostock, quotes cases to show that there is a close relationship between hyperthyroidism and war oedema. He alludes to the success obtained by administration of thyroid extract in many cases of war oedema and mentions the autopsy findings of Oberndorfer (vide *Medical Supplement*, 1919, **2**, 29), who found marked atrophy of the thyroid. He also alludes to Adler's experiments on hibernating animals as illustrating the connexion between diminution of food metabolism and the function of the thyroid. By injecting hibernating animals in which respiratory movements and temperature are reduced to a minimum, Adler succeeded in waking them after one to three hours and raising their temperature from 8° C. to 35° C. Hinz suggests that in war oedema the insufficiently nourished organism endeavours in like manner to protect itself by a diminution of thyroid function.

Stoeltzner reports the cases of three women who developed signs of hyperthyroidism in pregnancy, such as loss of appetite, constipation, obesity, loss of hair, dryness of skin, drowsiness, and indifference, and all gave birth to Mongolian imbeciles. On the other hand, in seven other cases of Mongolism there was no history of thyroid insufficiency during pregnancy. Stoeltzner, however, has published the cases in the conviction that positive results are of more importance than negative, and especially for the purpose of practical therapeutics. If mongolism is due to hyperthyroidism in the mother during pregnancy, thyroid opotherapy will not only cure the mother but will also prevent the birth of a Mongolian imbecile.

In a statistical study of myxoedema and cretinism in the United States and Canada, based on cases recorded in the literature from July 1, 1905, to July 1, 1918, Anders emphasizes the following points regarding myxoedema, of which he has collected 62 cases: (1) The remarkable frequency with which myxoedema is overlooked and is mistaken for chronic nephritis and other morbid conditions. (2) The close relationship between myxoedema and rapid child-bearing, pregnancy, and the menopause. (3) The acute infections, especially influenza, as points of origin for the condition. (4) The occasional association with myxoedema and disturbances of other endocrine organs than the thyroid, e. g. Addison's disease in one and pituitary disease in two of his cases. (5) The specificity of thyroid medication and the necessity of employing this agent in small doses to avoid toxic effects. (6) The importance of directing measures to any complications present, and near and remote aetiological influences in individual cases.

With regard to cretinism, of which he has collected 73 cases, Anders's conclusions are as follows: (1) Further growth of our knowledge of the aetiology is desirable, despite the close relationship with myxoedema. (2) Cretinism is relatively commoner in the male than myxoedema, owing mainly to the predominating connexion of myxoedema with the female genital organs. (3) A decreased basal metabolic rate from any cause exercised a slight though definite predisposing influence. (4) The frequent observation that cretinism may be an inheritance from goitrous antecedents receives confirmation from statistical studies. (5) Thyroid preparations are less effective in cretinism, particularly in the psychic manifestations, than in myxoedema, but are more beneficial to the mental condition if given in the earlier stages.

Murray relates the life-history of the first case of myxoedema treated by thyroid extract. As a result of its regular and continued use the patient was enabled to live in good health for over 28 years (April 1891 to May 1919), death being due to cardiac failure at the age of 74. During this period she consumed over 9 pints of liquid thyroid extract or its equivalent prepared from the thyroid glands of over 870 sheep.

Starr has found that the dryness of the skin, brittleness of the nails, and loss of hair usually met with in old age may be stopped by taking small amounts of thyroid (not more than 1 gr. of the Burroughs and Welcome extract) in divided doses in a day. The patients also feel more active mentally and physically, and suffer less from depression and insomnia. Starr concludes that some of the conditions supposed to be due to old age are actually due to a diminution in the activity of the thyroid gland and consequently may be obviated or removed by the constant use of thyroid extract as age advances.

Porak has found that injection of thyroid extract in myxoedema does not have a definite physiological effect, whereas in normal subjects it causes hypotension and acceleration of the pulse. In two myxoedematous patients, who were still under the influence of treatment, there was a suggestion of physiological reaction which was completely abolished when the treatment was discontinued for a longer period. He also found that adrenalin and extract of the suprarenal medulla had a more powerful action in normal subjects than in myxoedema. On the other hand, extract of the posterior lobe of the hypophysis had a much more active effect on the blood-pressure of myxoedematous patients than of normal subjects, as was shown by a sudden and prolonged fall of blood-pressure. By application of these glandular tests to various complex syndromes, Porak shows that it is possible to confirm or exclude the diagnosis of thyroid insufficiency.

L. Strauss reports a case of diabetes insipidus in a boy of 9, which gradually subsided in his 13th year and was replaced by clinical symptoms of myxoedema. At the age of 15, when the amount of urine had become quite normal, and the myxoedema was fully developed, he was given thyroid tablets, with the result that the myxoedema disappeared. Death from pneumonia occurred at the age of 20, but a necropsy was refused. Strauss has not been able to find another case on record of the conversion of diabetes insipidus into myxoedema. He suggests that the thyroid gland in his case was hypoplastic and that the anterior lobe of the hypophysis developed a compensatory enlargement which exercised pressure on the pars intermedia, and so gave rise to diabetes insipidus. As the pituitary enlargement subsided, myxoedema developed, which had hitherto been prevented by the vicarious action of the hypophysis.

Parathyroids. Cordier relates the case of a man, aged 41, suffering from chronic diarrhoea, intense cachexia, profound and progressive asthenia, paroxysms of cervical and prelaryngeal pain and tetany of the upper limbs. The autopsy showed a haematoma of the tracheo-thyroid space, which had destroyed the right parathyroid and haemorrhages in the left parathyroid. Nothing abnormal could be found in the other glands of internal secretion, and there were no haemorrhages elsewhere. The patient was not a subject of haemophilia, so that the cause of the haemorrhage was obscure. During the first stage of the disease, which probably corresponded to the occurrence of small haemorrhages in the gland, distinct improvement followed the administration of fresh parathyroid, but the treatment completely failed during the apoplectic stage.

Lange, of the Lubeck Children's Hospital, encouraged by the results obtained by transplantation of the parathyroid in post-operative tetany, performed the operation in four infants suffering from tetany; but the results were not encouraging. In three cases no improvement occurred, and in one the result was doubtful.

Suprarenals. A case of recovery from Addison's disease is reported by Giraudeau. The patient, a man aged 39, the subject of chronic alcoholism, was admitted to hospital in November 1901 with pronounced asthenia, pigmentation of the skin and buccal mucous membrane, diarrhoea, abdominal pain, and a feeble pulse. On January 4, 1902, he was given his first injection of suprarenal extract, and the injections were continued for 12 days. Improvement took place in the general condition, and there was a rapid increase in weight. The injections were resumed on January 27, when the abdominal pain and diarrhoea were very violent. On February 1 the pigmentation had considerably diminished in the face, and in the next two months disappeared from the rest of the skin and from the buccal mucous membrane. In the summer of 1902 the general condition had so much improved that the patient was discharged. Apart from an attack of alcoholism, for which he was interned in an asylum in June 1904, he was lost sight of until February 1913, when he was admitted to the asylum again with another attack. Death took place on March 13, 1913. Apart from carcinoma of the pylorus with metastases in the liver, the only lesion found *post mortem* was some scar-tissue in the right suprarenal indicating the occurrence many years previously of some inflammatory condition, the nature of which could not be determined. There were no signs of tuberculosis or syphilis. The case thus illustrates how a small suprarenal lesion is sufficient to give rise to the melanodermic syndrome. Giraudeau concludes that in cases in which transient suprarenal incompetence is the result of a localized inflammatory lesion treatment may be effective, whereas it is of no avail in caseous tuberculosis of the suprarenals.

Damade records the case of a man, aged 58, who presented intense asthenia, low blood-pressure, the phenomenon of the white line, digestive disturbances, and lumbo-abdominal pain accompanied by very slight pigmentation of the skin and mucous membranes. Treatment consisted in two subcutaneous injections of ½ mg. of adrenalin and 10 c.c. of glycerinated suprarenal juice by mouth. Immediate improvement resulted and the adrenalin was stopped in two days' time, but a relapse occurred a few days later, and death took place after a comatose period of five to six hours. Although the kidneys were studded with gross tuberculous lesions, it was only by microscopical examination that slight inflammatory lesions were found in the medulla of the suprarenals.

Lampl records a case of Addison's disease in a woman, aged 24, associated with cirrhosis of the suprarenals, vascular hypoplasia, and a persistent thymus. The uterus and mammae were of an infantile type and there was an increase of connective tissue in the thyroid and ovaries.

According to Mauclaire, who records an illustrative case, Apert in 1910 collected 30 cases of suprarenal hypertrophy or tumours of the suprarenal cortex which had given rise to a masculine appearance in women. Blanchard, in 1916, in a study of the pathogeny of suprarenal virilism, came to the conclusion that this condition was due to changes in the interstitial gland of the ovary, an opinion shared by Pierre Marie. Symptoms of virilism may also appear at the menopause, but they are not so marked as in suprarenal virilism. Mauclaire's case was a woman, aged 38, who six years previously had developed an abdominal tumour, and at the same time had cessation of her monthly periods. Her face, neck, and chest became covered with numerous long hairs, the face became elongated, the breasts atrophied, and the body lost its rounded form. Laparotomy revealed the presence of a tumour of the right suprarenal. The patient was subsequently treated with ovarian extract and her catamenia reappeared.

Dubois, assistant at the Berne University Pathological Institute, states that special attention has recently been paid there to the condition of the thyroid in Addison's disease. He records six cases, in four of which there was an extensive development of true lymphatic tissue with typical germ centres which might be regarded as abnormally situated new growths. According to Dubois, these growths are not of an inflammatory nature, but are the result of stimulation caused by suprarenal insufficiency and a consequent abnormal call upon the thyroid. He suggests that the formation of large follicles with germ centres is connected with the status lymphaticus, which is also present in Addison's disease.

According to Cosmettatos, who records a case of hydrocephalus and atrophy of the suprarenals in a child who died 24 hours after birth, cases of coexistence of malformation of the brain and suprarenals may be divided into two groups, namely, those in which the congenital anomalies occur at the commencement of development of the nervous system, and congenital anomalies which occur later, that is, after the appearance of the sympathetic ganglia and the chromaffin substance. In the first group the arrest of development of the nervous system entails an arrest of development of the sympathetic ganglia and consequently of the chromaffin substance also. In the second group, some morbid condition in the parents, such as syphilis, tuberculosis, or alcoholism, is responsible for the congenital anomalies in organs embryologically allied, namely, the brain and the suprarenal medulla.

Hypophysis. Acromegaly of late onset is exceptional. Examples of the kind have been recorded by Widal, Ballet, and Laignel-Lavastine, to which may be added the case recently reported by Hamant and Caussade. The patient was a woman, aged 53, the mother of 3 children, in whom the first symptoms, enlargement of the hands and feet, had appeared at the menopause four or five years previously. Subsequently the skin of the face and neck grew thick. Deformities of the trunk, visceral signs, and symptoms of compression were absent, but the diagnosis of acromegaly was confirmed by the X-rays, which showed enlargement of the sella turcica.

Fliess describes a syndrome characteristic of insufficiency of the anterior lobe of the hypophysis and consisting of five principal symptoms, viz. (1) general fatigue, (2) lack of power of concentration, (3) polyuria occasionally accompanied by enuresis, (4) occipital neuralgia, not unfrequently accompanied by backache and sciatica, (5) disturbances of menstruation, especially menorrhagia. The first four symptoms, though most frequent in women, especially during pregnancy, may also be found in the male sex at puberty. All the symptoms may be caused to disappear by administration of tablets made from the anterior lobe. Fliess emphasizes the importance of examining all the other members of the family to which the patient belongs for similar disturbances.

Reverchon, Worms, and Rouquier report a case of the adiposo-genital syndrome in a man aged 27, who presented symptoms of pituitary tumour, viz. obstinate headache, considerable diminution of visual acuity with homonymous temporal hemianopsia and bilateral optic atrophy. Although the ocular symptoms were permanent, considerable improvement in the adiposo-genital syndrome occurred under X-ray treatment of the hypophysis.

A case of *onychauxis,* or overgrowth of the nails of all the fingers and toes, is recorded by Hollander in a boy aged 9 years, who presented signs of dystrophia adiposo-genitalis. The carbohydrate tolerance was high, and the X-rays showed a small sella turcica with hypertrophy of the anterior and posterior clinoid processes.

Pineal gland. Jelliffe states that the metabolic disturbances attributed to disease of the pineal gland are: (1) fatty metabolism factors, obesity; (2) sexual precocity factors, macrosomia genitalis; (3) muscle metabolism, dystrophy factors; (4) mixed syndromes. He considers, however, that the fatty metabolism factor should be more definitely relegated to the hypophyseal function. Whether macrogenitosomia or sexual precocity depends upon pineal-gonadal interrelationship or a pineal-gonadal adrenal cortex complex as a primary pineal syndrome is not yet established, but macrogenitosomia seems to stand in closer relationship, especially in the young, to primary pineal function than obesity. Jelliffe agrees with Timme in the view that disturbances in the pineal gland play an important part in the pathogeny of progressive muscular dystrophy, this view being based partly on clinical signs and partly on the appearance of pineal shadows in the skiagrams of the patient's skull.

Berkeley has found that fresh preparations of pineal gland from calves and young cattle accelerate the growth of kittens, rabbits, and guinea-pigs to a marked degree, and that backward children without organic stigmata, to whom the gland is administered for a sufficient period—usually 3–6 months—showed a considerable acceleration in their mental progress. He has also found that the pineal gland preparations quicken the slowed down processes of old age, improve the memory, and produce a remarkable cheerfulness and sense of well-being.

Pluriglandular syndromes. Engelbach discusses arterial hypertension associated with endocrine dyscrasia in a paper based on 500 uncomplicated cases of endocrine disease, cases in which nephritis or arteriosclerosis were suspected being excluded. 46, or nearly 10 per cent., had a systolic pressure of 160 mm. Hg or above. Arterial hypertension was found to be most frequent among the polyglandular dyscrasias. 14, or 30 per cent., had more than one gland involved. Combined pituitary and thyroid hyposecretion was present in 12 cases. The next highest percentage, 11 cases, or a quarter of the whole number, occurred at the menopause, as in the cases reported by Riesman (vide *Medical Science* 1920, **2**, 216). The next in frequency was the thyroid group, with 8 cases, or 17 per cent., classified as pure hypothyroids and 4, or 8 per cent., as hyperthyroids. The pituitary group ranged lowest in number, 5 cases, or 11 per cent., being classified as simple dyscrasias of this gland. The prognosis is much more favourable in these cases than in those in which there is a high arterial tension due to definite vasculo-renal lesions. It is true that many of them develop arterial disease sooner or later, and others possibly renal disease. If the arterial tension is not reduced, many of the cases succumb to cerebral haemorrhage or cardiac incompetence. Treatment depends upon the nature of the internal secretory dyscrasia and is entirely different from that of nephritic or arteriosclerotic hypertension. Thus low protein and salt-free diet is frequently contra-indicated, whereas drugs such as epinephrin or pituitrin, which are contra-indicated in other types of arterial hypertension on account of their vaso-constrictor effects, are really applicable.

The fluctuations of thyro-suprarenal activity in general diseases are discussed by Sajous, who alludes to the suprarenal failure occurring in asthma, heart failure following acute infections, such as influenza and pneumonia, especially in old persons, and in tuberculosis. In 1903 he had suggested that strychnin owed its powerful influence on the oxygen intake and carbonic acid output to stimulation of the adrenals, a suggestion which has recently been confirmed by the investigations of Stewart and Rogoff, who found that therapeutic doses of strychnin caused a marked and lasting increase in the production of adrenalin.

Sabrazès and Dupérié report the case of a woman aged 29, the daughter of a goitrous mother and alcoholic father, who, in addition to hydrocephalus, presented a congenital thyro-ovarian insufficiency which was improved by opotherapy. But a deep goitre and a large thymus were refractory to treatment, and contributed to a fatal termination of an attack of typhoid fever. Examination of the glands of internal secretion *post mortem* showed normal parathyroid tissue and a hypophysis which was in a state of excessive activity. Sclerotic changes in the choroid plexus and various ependymal changes appear to have played an important part in the mechanism of hydrocephalus.

Étienne and Richard, who had previously recorded two cases of late epilepsy associated with disturbances of the glands of internal secretion, report another case in a woman aged 30, who, eight days before the end of her second pregnancy, was seized with a convulsive attack. No albumin was found in the urine, and eighteen months later symptoms of myxoedema developed, the monthly periods became scanty, and convulsive attacks occurred. Suprarenal involvement was shown by adrenalin glycosuria, and X-rays revealed enlargement of the hypophysis. Treatment by thyroid and ovarian extracts was instituted, and no further attacks took place.

In the treatment of backward children, Apert has found that better results are obtained by the addition of very small doses of suprarenal extract to the thyroid extract than by thyroid extract alone, especially when the children are thin, weak, and anaemic. There is then less risk of provoking tachycardia, emotivity, general excitement, and loss of flesh, which sometimes necessitate the stopping or at least the reduction of thyroid treatment. If the sexual development is out of proportion to the general bodily development, Apert recommends the addition of pituitary extract to the thyroid and suprarenal medication, or suspension of the latter. He has obtained good results from polyopotherapy in the treatment of Mongolism and debility following infectious diseases or underfeeding, as in the case of the children in the occupied regions of France during the war.

Cases of alopecia of emotional origin, and attributed to endocrinic disturbance, are reported by Étienne and Drouet and Todde respectively. Étienne and Drouet's case was that of a boy aged 12, who lost all the hair of his scalp, eyebrows, and eyelashes, after a fright caused by an air raid. In Todde's case, which occurred in a man aged 34 following emotion and war strain, the alopecia was complete and generalized, and was accompanied by enlargement of the thyroid, exophthalmos, tachycardia, and some enfeeblement of sexual activity.

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J. D. R.

CEREBROSPINAL FEVER

Epidemiology. According to Reece the number of cerebrospinal fever cases which occurred in the civil population of England and Wales during the three years 1914 to 1916 was 300, 2,343, and 1,278 respectively. In 1917 1,393 cases were known to have occurred. In 1918 the number of recorded cases fell to 715, and in this year there was also a considerable decline in the total number of cases which occurred in the army. There were many cases in 1917 and 1918 in which it seemed probable that the infection was introduced into the household by a soldier returning home on leave from camps in this country or overseas. Repeated occurrences of the disease breaking out after the soldiers' arrival gave an accumulated value to the evidence. In certain instances examination of the soldiers by military bacteriologists gave positive results.

As the special circumstances which favoured the spread of infection of cerebrospinal fever during the last five years are no longer operative, Reece thinks it probable that the excessive prevalence of the disease among the civil population which marked the period of the war will cease, and that there will be a reversion to the incidence of peace times.

Cases of cerebrospinal fever arising after return home of soldiers who were meningococcus carriers are reported by Nammack and Shaw. In Nammack's case the soldier was discharged from an isolation hospital in France after three negative cultures of the throat had been obtained, but six months later infected his six months' old baby at his home in the United States, when nasopharyngeal cultures were again found to be positive.

Nammack thinks that though the carrier does not constitute a grave menace in civil life except in time of epidemics, in military life he is an important factor in the spread of the disease. The mere finding of three negative cultures does not, in his opinion, constitute a proof of the continued sterility of a carrier, but the patient should be examined again after an interval and treatment re-instituted if necessary. Shaw's case occurred in a five months' old baby which was infected by its uncle, a healthy carrier, who had not, to his knowledge, been in contact with cases of cerebrospinal fever or had the disease himself. Shaw concludes that so-called sporadic cases are in reality untraced cases, and that the human carrier is responsible for cases appearing either singly or in epidemics.

Symptomatology. Lustig, of the Pressburg Children's Clinic, records the case of a girl aged 8 years who developed a **relapse** of cerebrospinal fever three weeks after recovery from the primary attack. A fresh infection could be excluded, as no other cases of cerebrospinal fever had occurred for a long time at the clinic. Lustig attributes the relapse to the patient having lost the passive immunity which rendered her insusceptible to the meningococci still present in the system after recovery from the primary attack. He therefore recommends that treatment should not be discontinued as soon as the cerebrospinal fluid becomes clear and the meningococci disappear from it, but that urotropin should be given internally and the nasopharynx painted with a disinfecting fluid during convalescence.

A fatal relapse ten weeks after recovery from the original attack is reported by Randall in a man aged 33. In both attacks the meningococcus was isolated from the cerebrospinal fluid, and the treatment consisted in lumbar puncture and administration of antimeningococcal serum.

In a paper based on the study of 321 cases of meningococcus infection at Camp Jackson, N.C., where arthritis was an unusually frequent complication, Herrick and Parkhurst describe three forms of **meningococcus arthritis,** which they designate as 'Type A', 'Type B', and 'Type C' respectively. Type A is an acute polyarthritis, which is frequently the initial symptom and rarely appears later than the first, second, or third day of the disease. It is almost always associated with purpuric haemorrhagic rashes, and appears to be due to haemorrhage into the articular and periarticular structures. It is frequently accompanied by other complications of meningococcal sepsis, e. g. panophthalmitis, epididymitis, and pericarditis. Its duration is usually from one to six days. In exceptional cases the arthritis may be prolonged for several weeks and may then merge into Type B. Twelve examples of Type A occurred among the 321 cases, with four deaths or a mortality of 33·3 per cent. The onset of Type B is late, usually about the fifth day. With rare exceptions only one joint is affected. The exudate is usually viscid, mucinous, or semi-purulent, not unfrequently haemorrhagic. Meningococci are found in at least one-third of the cases. Systematic disturbance in the form of moderate fever is usually present. The process generally lasts one to four weeks, recovery being gradual but complete. The prognosis is good, only two of the 16 cases belonging to this type died. Type C is the ordinary serum arthritis, of which there were twelve examples in this series.

Serr and Brette record two cases of unilateral non-suppurative **parotitis** occurring at the end of an attack of cerebrospinal fever, and regard the complication as the result of a blood infection rather than of an ascending infection from the mouth. They allude to a case of meningococcal septicaemia recently reported by Lemierre and Lantuéjoul, in which parotitis was associated with orchitis and thyroiditis (vide *Medical Science*, 1919, **1**, 135).

Käding records two cases in children, one of whom had had fifty lumbar punctures performed and 817 c.c. of cerebrospinal fluid evacuated, who showed an extreme loss of flesh, although the temperature was normal and they were taking nourishment well. This condition, which has been designated 'meningitis cachexia' by Schottmüller, is attributed by Käding to a disturbance of all the glands of internal secretion caused by a damage to the hypophysis.

Beaussart records a case of meningococcal cerebrospinal meningitis secondary to suppurative otitis in a young soldier suffering from scarlet fever. Recovery followed lumbar puncture. The cases show the importance both from the therapeutical and prophylactic standpoint of examining the cerebrospinal fluid in such cases. The meningeal symptoms might otherwise have been regarded as a complication of otitis media, especially as no case of cerebrospinal meningitis had recently occurred in the garrison.

According to Sabrazès (1), of Bordeaux, the **co-existence of tuberculous and meningococcal infection** is not an exceptional event. Out of a total of 495 cases of meningitis in adults treated in his infectious service from 1914 to July 1919 there were 350 cases of meningococcal meningitis, 56 of tuberculous meningitis, and 7 or 1·41 per cent. of combined tuberculous and meningococcal meningitis. In these cases of combined tuberculous and meningococcal meningitis the cerebrospinal lymphocytosis characteristic of tuberculous meningitis continues to be pronounced in spite of the polymorphonucleosis due to meningococcal infection and the intrathecal injection of substances which stimulate a polymorphonuclear reaction. Sabrazès concludes that apart from the discovery of the tubercle bacillus in the cerebrospinal fluid, which occurs in only one-third to a quarter of the cases, and animal inoculation which requires too long a time, irreducible lymphocytosis is one of the best means of diagnosis in combined tuberculous and meningococcal infection. Other diagnostic features characteristic of concomitant tuberculous meningitis are the progressive oliguria in contrast with the polyuria of uncomplicated cerebrospinal meningitis, the persistence of fever in spite of the disappearance of meningococci from the cerebrospinal fluid under the influence of serum treatment, vasomotor flushes of the face, irregular temperature, hiccough, and xanthochromia of the cerebrospinal fluid.

Claude, Schaeffer, and Bernard record a case in a man aged 54, in whom the diagnosis of combined tuberculous and meningococcal meningitis could be made during life by finding the two organisms present in the cerebrospinal fluid. The clinical picture was that of cerebrospinal meningitis or rather of meningococcal infection in which articular localization at the onset preceded the meningitis. The necropsy showed lesions of subacute tuberculous meningitis rather than those of cerebrospinal meningitis. The absence of pus and predominance of lesions at the base of the brain were not in favour of the latter. Lastly, histological examination did not show granulations or tubercles, and the condition appeared to be an example of atypical tuberculosis of the meninges in which ordinary inflammatory lesions predominated. In these cases of mixed meningitis the tuberculous infection as a rule appears to be primary, and the meningococcal infection secondary. The prognosis is almost invariably fatal owing to the existence of tuberculous infection. A transitory improvement, however, is occasionally observed, as in the case reported by Claude, Schaeffer, and Bernard, after serum treatment.

Meningococcal septicaemia. Sudeck suggests the substitution of the term 'meningococcal general infection' for 'epidemic meningitis', the former term including the following conditions: (1) cases with symptoms confined to the meninges; (2) cases with more or less marked symptoms of septicaemia which are usually prodromal and later accompany the meningitis; (3) cases with more or less marked prodromal septic symptoms which are followed later by meningitis; (4) cases with more or less marked septic symptoms and an entire absence of meningitis.

Ribierre, Hébert, and Bloch record seven cases of meningococcal infection, in three of which there was no meningitis at all, and in four the meningitis did not occur till a later stage. The clinical picture was characterized by three principal symptoms: (1) fever of a malarial type; (2) an eruption which was most frequently papulo-nodular in type, but was sometimes macular like that of typhoid or typhus, or petechial or purpuric; (3) arthropathies.

Netter, Salanier, and Strauss record a case of generalized purpura in a girl aged 11 years associated with uncontrollable vomiting, abdominal pain, and haemorrhagic diarrhoea. In spite of the absence of meningeal symptoms Netter diagnosed meningococcal septicaemia and antimeningococcal serum was injected intrathecally and intramuscularly with rapid improvement. Cultures of the blood and cerebrospinal fluid were negative, but smears obtained by scarification of the purpuric patches showed the presence of meningococci. In convalescence the child developed a perforation of the cartilaginous part of the nasal septum at the site of an old patch of purpura. The occurrence of abdominal pain, vomiting, and bloody stools showed that purpuric lesions were also present in the intestine as in Henoch's purpura and angioneurotic oedema.

Prognosis. According to Raisin the prognosis of cerebrospinal fever is worst at the extremes of life (infancy and old age) and when the disease is associated with other morbid processes, especially alcoholism or strain. Generally speaking, all symptoms indicating depression are more serious than those of excitement. Apart from purpura, which indicates a very severe form of septicaemia, no single clinical system is sufficient to establish a prognosis. The following prognostic data are obtained by study of the cerebrospinal fluid: (1) The amount of pus in the fluid has no prognostic value, but its rapid disappearance as the result of treatment indicates a more or less favourable case. (2) Yellow coloration or xanthochromia of the cerebrospinal fluid is characteristic of severe forms, and indicates an unfavourable course. (3) The absence or scarcity of meningococci in the smears and cultures of the fluid withdrawn in the early stage is only found in cases which recover rapidly. On the other hand the presence of very numerous meningococci in smears and cultures at the onset of the disease is chiefly seen in fatal or prolonged forms. (4) The diminution of polymorphonuclear cells, the substitution of healthy for damaged cells, and the appearance of small or moderate mononuclear cells and endothelial cells are favourable signs. (5) The amount of albumin diminishes in favourable cases, and remains high or increases in severe cases. (6) The sugar which has disappeared or diminished at the onset reappears in the fluid at about the fifth day. Its absence is the sign of a complication or relapse.

According to Servais recovery from cerebrospinal meningitis after four or five injections of antimeningococcal serum appears to be less frequent than formerly, especially in the adult. He describes the following changes in the classical type of the disease to which he attributes the failure of serum treatment, even when it is employed early and in large doses: (1) The frequency of relapses, the prognosis of which is very grave owing to the likelihood of fatal anaphylaxis, the resumption of serum treatment being required at a time when anaphylaxis is most likely to occur. (2) The frequency of septicaemic forms, especially of purpura, the prognosis of which is also very grave. (3) The frequency of reactivation of old latent brain lesions. This fact is very important at the present time in view of the large number of persons who are suffering from injuries to the brain, and who are liable to have them infected or roused into fresh activity by meningococcal infection. (4) The association of the meningococcus with the pneumococcus, the virulence of which has been constantly exalted during the last few years until it has reached its height during the epidemic of influenza.

Sabrazès, whose article on the renal complications of meningococcic injection was recently abstracted (vide *Medical Science*, 1919, **1**, 136), states that the prognosis in cerebrospinal fever often depends upon the integrity of the emunctories, previous disease of the kidneys or liver often proving an aggravating factor. He records an illustrative case in a man, aged 30, complicated by cholaemia, azotaemia, purpura haemorrhagica, and haemorrhage in the cerebrospinal fluid, whose death was due to uraemia.

Treatment. Haden, who, like Herrick, regards meningococcus meningitis as primarily a generalized infection with subsequent meningeal localization, considers that the intravenous use of immune serum marks a great advance in the treatment of the disease. He maintains that prolonged intrathecal treatment is very apt to result in permanent ill effects from involvement of the cauda equina and nerve-roots. Intravenous treatment, on the other hand, decreases the number of intrathecal injections and thus minimizes their harmful effects. He records a case in which an active localized infection in the meninges recovered under intravenous therapy alone.

Lewkowicz regards the lateral ventricles as the principal site of infection in cerebrospinal meningitis, and therefore recommends that the injections of serum should be made directly into the ventricles; a dose of 10–20 c.c. of antimeningococcal serum should be given into both ventricles every three days. As a rule the serum should not be given after the second week dating from the first injection. Lewkowicz reports a series of 22 cases—10 in children from two years and upwards, and 12 in adults—treated by intraventricular injections with eight deaths, or a mortality of 36·3 per cent.

According to Banks, with a little more experience a fairly reliable clinical classification according to Gordon's four types of meningococcus may be arrived at. The observations of Kennedy and Drought suggest that Types 1 and 3 (Nicolle's Type A) are more virulent as regards the meninges, and that Types 2 and 4 (Nicolle's Type B or parameningococcus) are specially prone to cause septicaemia and extrameningeal metastases. Banks records two cases successfully treated by Type 1 serum. The use of monotypical serum is also recommended by Munro, who records 13 illustrative cases. Of 10 cases treated by monotypical serum 8 recovered. No cases that lived long enough for the type to be determined died.

In cases of meningococcal infection Ribierre, Hébert, and Bloch recommend that the causal organism shall be identified as soon as possible, so that a rigorously specific serum may be employed early. While waiting for its identification a polyvalent serum should be used. The treatment should be commenced by a series of five injections of 40 c.c. of serum given at 24-hour intervals by the subcutaneous and intramuscular routes alternately. If during the following days no improvement occurs, the intravenous method should be employed, with precaution against anaphylaxis. If this fails, the serum should be given intrathecally, even if there are no symptoms of meningitis. As a rule, one to two injections of 30 c.c. each will suffice.

Méry and Girard point out that though serotherapy has always been the method of choice in the treatment of cerebrospinal meningitis it proves inadequate under the following circumstances : (1) when there is an ear complication present ; (2) when the meningitis is due to an atypical organism ; (3) when the patient does not tolerate the serum treatment well ; (4) when the meningitis has a chronic course with or without a tendency to meningococcal septicaemia. They record a case of meningococcus C septicaemia with ill-developed meningeal symptoms in which, owing to the occurrence of anaphylaxis, vaccine treatment by an autovaccine injected subcutaneously was substituted for serum and was followed by complete recovery. The writers recommend the systematic employment of combined serum and vaccine treatment from the onset in every case of cerebrospinal meningitis as likely to improve the prognosis and prevent complications.

Sergent, Provost, and Bordet also report a case of meningococcus C septicaemia without any meningeal involvement which was cured by intravenous injection of a stock meningococcus C vaccine.

Lewkowicz considers that vaccine treatment is indicated from the first in addition to serum-therapy. He points out that the value of vaccine treatment is shown principally in severe cases which have no tendency to spontaneous recovery.

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J. D. R.

TRANSFERENCE OF THE CORRESPONDING FIBULA TO REPLACE THE DIAPHYSIS OF THE TIBIA, WHICH HAD UNDERGONE NECROSIS

Brandes, of Kiel, treated five cases in which the diaphysis of the tibia had undergone necrosis by transferring the corresponding fibula into the position previously occupied by the shaft of the tibia.

His paper includes a criticism on operations to repair the results of necrosis following gunshot wounds. But his essential contribution concerns the question whether there is a method of treatment superior to amputation.

Case 1. A boy, in 1906, was attacked by acute infective osteomyelitis of the right tibia, which was followed by necrosis of the diaphysis. He was operated upon several times for the removal of sequestra. In 1908 he fell and fractured the weak newly-formed tibial diaphysis, at the same time the head of the fibula was subluxated. There was abnormal mobility and the tibia under the X-rays showed a defect of 7 cm. in length. The leg was both shortened by 8 cm. and curved; right leg length 28 cm., left leg 36 cm.

In 1909, bone from the humerus and femur of an infant which had died during birth was at once transplanted to connect the two ends of the tibia. Four months later an X-ray examination showed that both grafts had become reabsorbed. Thereupon the fibula of a boy killed in an accident was grafted in. This graft necrosed and was subsequently removed.

In 1910 there was a defect in the tibia 12 cm. in length. The patient could only move about with the leg in plaster. Now, following the example of others, including Hahn in 1884, the upper end of the fibula was cut across below its head, and the cut end driven into the upper end of the tibia. A haematoma with limited suppuration followed; in 1912 it was necessary to remove some more dead bone; nevertheless there followed firm union between the upper end of the tibia and the fibula. But the fibula had then to bear all the weight in an oblique line from within outwards to the external malleolus, which had no firm bearing, and there was therefore a tendency to pes varus. Thus there was no improvement in the limb from the functional point of view. Hence, seven months after the upper implantation, the lower end of the fibula was cut across above the external malleolus and implanted into the lower end of the tibia. Healing occurred and the patient was able to get about.

The boy was re-examined in 1919. He had for the last four years not worn any splint; the foot had ceased to swell, he could walk about for several hours without the leg getting tired. Indeed he could keep about on his legs all day and also could work as a tailor, sitting with his legs crossed. The scars were sound. The leg was 10 cm. shorter than the sound one; there was slight varus; the knee-joint moved freely, the ankle-joint allowed of flexion and extension to about half the usual extent. With a high-soled boot he walked without apparent lameness.

Case 2. A girl at the age of 8, in 1907, had acute osteomyelitis of the left tibia; she was operated upon repeatedly and sequestra removed. In 1909, when aged 10, the leg was atrophied and shortened; there was abnormal mobility in the shaft of the tibia and a defect for a handsbreadth. The movement of the knee-joint was limited between 180° and 140°, the ankle-joint was stiff, the toes pointing slightly. From a limb which had been amputated on account of an accident, a graft from the tibia was inserted into the defect. The transplant underwent necrosis and was removed eight months later. In 1911 there was a gap in the tibia 8 cm. in length; then the upper end of the fibula was fixed into the head of the tibia. It united firmly. But owing to the oblique line of the axis of the fibula carrying the weight, the use of the limb had not improved. Therefore in 1912, fourteen months after the implantation of the upper end, the lower end of the fibula was fixed into the lower end of the tibia. After healing the leg was put up in plaster.

When re-examined in 1919, the girl being then aged 20, she was wearing a boot and splints; she found that the splints kept her foot from swelling. She could keep on her legs all day; in previous winters there had been pain with changes of weather, but she had lost this complication during the last winter. The scars were firm, without inflammation, and most of them were movable. The continuity of the leg was solidly firm. The shortening of the leg was 9 cm., right leg 42 cm., left leg 31 cm.; the total length of the lower limbs was, right 84 cm., left 74 cm.; so that disuse had resulted in a shortening of the femur on the affected side by 1 cm., the total shortening being 10 cm. Circumference of calf, right 29 cm., left 24 cm.

Case 3. A girl aged 5, in March 1914, had acute osteomyelitis with necrosis of the whole of the diaphysis of the tibia, which was removed in April 1915. In August 1915 there was a reproduction of the tibia, not thicker in the X-ray photograph than the fibula, and yielding especially in the upper third. Two sinuses were scraped and, after applying extension, the limb was put in plaster. In 1915 a graft was transplanted from the tibia of the opposite side into the gap. In 1916, nine months after the above operation, the leg was found markedly shortened and atrophic; the knee-joint was stiff, the leg below movable in all directions. The transplant had been completely reabsorbed; the upper end of the fibula was then inserted into the head of the tibia and, two months after this, the lower end of the fibula was implanted into the lower end of the tibia. In doing this, the periosteal sheath was made to surround the fibula, after removing any newly reproduced bone which was in the way. In 1918 the patient was wearing a high boot and splint. The X-ray examination showed a strongly developed shaft of bone replacing the tibia.

Case 4. In 1909 a girl aged 8 had necrosis of the diaphysis of the right tibia. In 1917 there was a defect in the tibia 20 cm. in length. The upper end of the fibula was implanted into the head of the tibia, and in 1919, eighteen months after the first operation, the lower end of the fibula was fixed into the lower end of the tibia. A renewal of the shaft of the tibia followed and was taking place at the date of the last report.

In carrying out these operations there are difficulties connected with the scars and sinuses. As a matter of fact this transference of the fibula is not so much endangered by the suppuration which causes the necrosis of free grafts. In carrying out the transference the tibial periosteal sheath is split, the upper and lower end of the tibia trimmed, and any newly-formed bone obstructing the transference is removed. The head of the fibula and the external malleolus are not disturbed. In transferring the fibula the muscles must be spared as far as possible.

The main question is whether the patient is better off than with an artificial limb after amputation. At any rate this transference of the fibula appears to be the method to adopt; free grafts from amputated limbs have proved a failure; to weaken the opposite tibia by grafting from it is objectionable, and the operation failed in Case 3.

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W. G. S.

ACTINOMYCOSIS

In this country actinomycosis is a rare disease; it is of much more frequent occurrence in France and Germany. Hence, although its clinical signs are fairly evident, there may be delay in diagnosis, especially when no previous case has been known to have occurred in the district. It has been asserted, for instance, that, as distinguished from madura foot, actinomycosis does not occur in India, yet in that country and in the same number of the *Indian Medical Gazette* Sur described three cases and Saha one case.

Another cause of delay in diagnosis is the failure to find the actinomycosis organisms. It is often a fact that these can only be discovered after repeated examinations; meanwhile, unfortunately, the disease may have become firmly established. In many cases clinical indications furnish earlier evidence than a microscopic examination of the discharge. There is besides a difficulty regarding nomenclature, the title adopted by the College of Physicians is Actinomycosis synonym Streptotrichosis. There is no mention of the term Nocardiasis, under which is included by some sporotrichosis or Infectious Granuloma. A typical case of the latter described by Guy differs from actinomycosis. The primary lesion on the finger is followed by the formation of a row of nodules up the line of the lymphatics of the arm, which break down into ulcers, clinically different from anything actinomycotic.

In the absence of any identification by the microscope, improvement under large doses of iodide of potassium is good clinical evidence, provided that the patient presents a negative Wassermann reaction. An early clinical diagnosis is of primary importance, not only in relation to the rapid cure of the primary lesion, but also in order to prevent local extension and metastases, which will ensure a fatal termination. Poncet's statistics exhibit the wide difference in mortality between the superficial and deep lesions; the mortality in actinomycotic cutaneous lesions being 2–3 per cent.; in superficial facial and cervical lesions, 10 per cent.; in deeper facial, cervical, and bone lesions, 30 per cent.; in intestinal lesions, 65 per cent.; in pulmonary lesions, 85 per cent.; in hepatic and cerebral lesions, 100 per cent. By some writers the serum agglutinating test of Widal and Abrami is considered of importance. Carious teeth should not be regarded as *par excellence* the point of entry of the organism. There need be no evidence of lesion in the mouth or fauces. Yet there have been described a number of facial and cervical cases of actinomycosis in which the organism entered by the parotid, submaxillary, sublingual, and salivary ducts. The first nodule has appeared in front of the ear or below the jaw. Christopherson and Archibald described a primary infection of a lacrimal gland, whence it spread into the upper lid.

Cutaneous infection of actinomycosis may be due to the organism being rubbed in through the intact skin. Cases occurred during the war to soldiers sleeping on straw. Three such cases were described by Quervain.

Case 1, aged 31. Began to sleep on straw at the beginning of August 1914; he entered hospital on the following October 3, with two deep abscesses, one in the right temporal region, the other in the outer side of the left thigh, both discharging actinomycotic pus. He was treated by limited incision and scraping, potassium iodide internally, and the application of drugs. The temporal abscess healed and remained healed. The abscess in the thigh was not healed when he was discharged at his own request. It subsequently deepened and extended laterally; metastases followed in the lungs, and he died on November 19, 1915.

Case 2, aged 31. Began to sleep on straw in Nov. 1916. On March 20, 1917, he presented a typical facial and cervical infection by actinomycosis on the left side. He had a carious left upper molar with some inflammation of the gum, also of the gum around the left lower molars, but the entry of the actinomycosis had not been that way.

Case 3, aged 23. Began to sleep on straw during the second week of March 1917. Fourteen days later he developed a typical cervical actinomycosis.

Two further cases were seen of similar origin. Petges and Darget noted that a soldier aged 45 was infected after sleeping on straw, also a comrade. The parotid submaxillary and cervical regions became involved in an induration spreading from the cheek. The induration was wooden in consistency, deeply fixed, and interspersed with nodules of a violet red colour and by several sinuses. There was marked improvement in the course of three weeks under iodide of potassium, 4 grm. a day. Brickner's case in a soldier was mistaken at first for tuberculosis of the hip. A red spot just above the left great trochanter was followed by enlargement of the glands in the groin, an extraperitoneal iliac abscess, an invasion of the ilium and of the left loin. The treatment consisted partly in local incisions and scrapings, but mainly in large doses of iodide of potassium. He took without harm as much as '700 grains', i.e. 45 grm. a day, later reduced to 4·5 grm. a day. He was cured after a year and a half.

Weiss, at a Medico-Chirurgical Meeting in the Northern French Army, described two cases in soldiers. One was a case of superficial submaxillary actinomycosis with several nodules and sinuses. The other had begun as an acute congestion of the left eye and swelling of the cheek extending to the left mandible, with fixture of the jaw and multiple abscesses in the cheek. The disease continued for three months before it was correctly diagnosed, and in that time an extensive involvement of the orbit had occurred.

1. **Treatment.** *Surgical excision* of an indolent nodule is always indicated, the more so if it is tending to soften in the centre. But if there is an induration with several nodules, the operation should be limited to incising, scraping out, and treating the interior with some form of iodine. In no case is a wide excision, whether of soft parts or bone, indicated.

2. *Internal administration of iodide of potassium.* This must always be started by giving large doses, at least 4 grm., and even that amount three times a day. These large doses are for a time well borne, and superficial complications such as acne should be ignored until a marked improvement has been obtained. It is necessary to persist with this iodide administration in smaller doses at intervals for an indefinite period to prevent recurrence.

3. *Local injection of iodine* into nodules, at various points into indurations, and into sinuses, also after incisions the dressings should be soaked with iodine. It does not appear to be established what is the best form of injection, tincture of iodine, iodoform, iodide of potassium in water. Razda especially emphasized the merits of the iodine and peptone combination

called iodon (Robin). It produced a maximum effect with a minimum of pain and local reaction. In 21 cases this remedy had not been used. Then he treated 5 cases with the addition of iodon (Robin) injections.

Case 1. Actinomycosis commenced in the left submaxillary region and spread to the neck, which became deeply infiltrated; three nodules broke down and formed sinuses. There was under treatment temporary improvement, then recurrence until iodon (Robin) was injected into the induration at various spots every two days. Rapid healing followed in the course of five weeks.

Case 2. An advanced case of pulmonary and hepatic actinomycosis had developed an abscess in the right hypochondrium with widespread induration of the abdominal wall. The case was treated by daily injections of iodon into the sinus left by the abscess and into the indurations. There was marked local improvement for four months, but the patient died from deep extensions in the abdomen and lungs.

Case 3. Actinomycosis attacked the appendix, which was removed; but this did not prevent local extension. After two months, iodon was injected locally, also it was administered internally, and later there were added X-ray exposures. Two years later the patient was in good health with sound scars.

Case 4. Actinomycosis of the right face failed to improve under other treatment until after two months, when iodon injections were begun, and healing followed in six months.

Case 5. A male aged 31 had infection of the left face and neck which communicated with the mouth and jaw; this healed in 7 months under treatment by the iodon local injections.

It is remarkable that iodine does not check the growth of actinomycosis in glass-cultures, and therefore may be supposed in the living tissues to play in some way the part of an activant.

4. *X-ray treatment* has come to be an important adjuvant, and in the case of cutaneous actinomycosis, also in clearing up remnants of induration in scars, it is of special service. In a case described by Wickhoff the skin and subcutaneous tissue were infiltrated by actinomycosis from the zygoma to the clavicle and from the nasolabial fold to behind the angle of the mandible on the right side. Nodules, softening in the centre, were scattered throughout the indurations, but no sinuses had formed. There were 10 exposures to the X-rays at intervals of a week, also iodide of potassium was given internally. Before the commencement of the treatment, actinomycosis was demonstrated in the nodules; as improvement set in, the organisms could no longer be found.

5. Radium was used successfully in 6 cases by Heyerdahl in Christiania.

Case 1. A male aged 32 with facial actinomycosis was under surgical treatment from November 30, 1912, to February 10, 1913, at the same time that iodide of potassium was administered internally. Radium treatment was begun on February 10, healing was complete on May 26, and the patient continued well.

Case 2. A male aged 17 with facial and cervical actinomycosis was under the same surgical treatment from December 1913 to February 25, 1914, when radium treatment was commenced and healing was completed by April 19. There was no recurrence after a year.

Case 3. A male aged 44, after surgical treatment for cervical actinomycosis, commenced radium treatment on May 4, 1915, and had healed by July 30.

Case 4. A male aged 79, affected with deep cervical actinomycosis, after surgical treatment, commenced radium treatment on January 15, 1914. He had healed by March 2 and remained so.

Case 5. A male aged 18 with facial and cervical actinomycosis, after surgical treatment, was treated by radium from December 9, 1915, and had healed by March 1, 1916.

Case 6. A male aged 27 with cervical actinomycosis was treated by radium from February 12, 1916. He had healed by March 28, and remained permanently healed.

6. *Autovaccination* has also proved an adjuvant, especially in aiding the closure of persisting sinuses. Malcolm described a case of pulmonary actinomycosis which had penetrated to the surface of the chest wall through the intercostal spaces. The patient was treated by incision, scraping, and removal of ribs, followed by the administration of iodide of potassium for months. Two sinuses persisted, one surrounded by induration being connected with the pericardium. Under vaccine therapy the sinuses gradually and definitely healed.

In Dean's case, a male aged 18 had had for 6 weeks an induration in the left parotid region with two sinuses, from which actinomycosis granules were obtained. After incision and iodide of potassium, 1 grm. *ter* for 6 weeks, there was only partial improvement. Four doses of autovaccine resulted in healing which remained definite.

Clinical varieties of Actinomycosis.

Cutaneous Actinomycosis. Not only may inoculation occur through a small wound of the skin, but, as noted in the case of soldiers sleeping on straw, there need be no noticeable previous lesion of the skin. Also extension on the skin may be due to auto-inoculation by scratching. The case described by Pringle furnishes an illustration of both the foregoing modes. A gentleman out hunting, having to defaecate, wiped his anus with straw. There followed a pustular eruption around the anus which spread into the rectum. Mercurial treatment failing, part of the anus and rectum was cut out and reported to be indefinitely epitheliomatous. There supervened lesions of the face and ear, and a boggy swelling under the chin became a crateriform ulcer. Pringle found that these lesions were due to actinomycosis, including the primary ones around the anus, from which the actinomycosis had been transferred to the face by scratching. The patient recovered in the course of a year under large doses of iodide of potassium. The peculiar extension in this case from a cutaneous to a mucous surface has been described on the Continent not only in the case of the lips and mouth, but also as an explanation of infection of the vagina and uterus and the male urethra.

Cutaneous actinomycosis affecting the face and neck, due to infection through the skin, should be distinguished from the deeper forms of facial and cervical actinomycosis. Syphilis being excluded, it has to be differentiated from lupus. Actinomycosis may be distinguished by a more rapid spread of woody induration, both in the skin and subcutaneous tissue, by the formation of discrete nodules scattered over the indurated area, which tend to soften in the centre, break down into sinuses with violet-red discoloration of the skin, and an undermining of the skin to form tunnels, which has given rise to a comparison with molehills. There is, besides, an early enlargement of lymphatic glands, and in some cases a rapid extension into the depth. Thus actinomycosis starting on the nape of the neck has quickly burrowed down to the spine.

Cutaneous actinomycosis is amenable to treatment, but this must be actively pursued. Further, it is necessary to keep a watch against recurrence for a long while, an insidious induration in a scar or the reformation of a sinus may be rapidly followed by a deep or metastatic extension.

Actinomycosis infection enters commonly *through the mouth*, settles, and infects—

a. The jaw through a carious tooth or beside the gum.
b. The tongue.
c. The fauces and glands of the neck.
d. The face and neck through the salivary ducts.
e. The gastro-intestinal tract, particularly the appendix.
f. The lungs, by inhalation, especially of dust.

a. The jaw. The presence of carious teeth and inflamed gums does not necessarily mean that the actinomycosis infection has actually entered that way. An involvement of the jaw increases the danger to life up to 30 per cent. Therefore active surgical treatment is necessary, the removal of carious teeth and the scraping away of dead bone. But a wide excision of the mandible should be rejected; it has proved either excessive or not enough. The excavation in the bone should be filled with gauze soaked in iodine or saturated with iodoform, and the other measures adopted, especially the administration of iodide of potassium and the local injection of all indurations around the mandible.

b. The tongue presents an indolent nodule, sometimes actually caused by a vegetable fragment penetrating. But there may be no history to confirm this. Such a nodule should not be left; syphilis being excluded, it should be cut out, when it will be found most probably to be due to inoculation, either by actinomycosis or tubercle. A somewhat more extensive lesion, a nodule, surrounded by induration, may be first explored and a bit cut out and examined by the microscope. Actinomycosis being discovered, the nodule and surrounding induration should be removed by a wedged-shaped excision, followed by suture.

If the tongue becomes widely infiltrated with softening at various points, no extensive excision of the tongue should be contemplated. Abscess formations should be incised and treated with iodine, the indurations injected in many places, iodide given internally, and perhaps the tongue submitted to X-ray or radium treatment.

This type of diffuse infiltration of the tongue and salivary glands of cattle by actinomycosis constitutes the most likely way of infection through food. Griffiths examined infected ox-tongues both from home cattle and those imported.

c. The fauces and glands in the neck. The inoculation in these cases is through the tonsil or some neighbouring crypt. It is generally impossible to find the actinomycosis organisms sufficiently early.

Apart from syphilis, the difficulty is to differentiate actinomycosis from cancer. The main distinction is the rapid development of the actinomycosis infection as compared with cancer. The following case may be cited as typical.

In March 1900 a farmer, aged 46, in good health, except for some carious teeth, began to suffer from difficulty in swallowing; a swelling formed in front of the left ear and another under the jaw. As the disease advanced the carious teeth were removed, but the dentist reported that the teeth were unconnected with the disease. The patient was seen within a month of the first commencement of his illness; from being a powerful man, he could not then stand alone, owing to loss of flesh and weakness. There was an indurated mass studded with nodules extending from the parotid region to the clavicle, deeply fixed, with about half a dozen sinuses, discharging a little foul pus, the sinuses having bluish margins. He could open the mouth only for ¾ inch; under an anaesthetic, there could be felt behind the palate a hard mass bulging in the lateral wall of the nasal pharynx and pharynx on the left side, which bled easily on being touched by the finger. The sinuses were lightly scraped and then treated with glacial carbolic acid.

In the scrapings were found yellow granules composed of streptothrix organisms, but which could not be positively identified as actinomycosis. The general practitioner had been all his life in the chief practice of a wide country district, and his father and grandfather before him. He said repeatedly, with confidence, that no case of actinomycosis, either in cattle or in man, had ever occurred in his district. The patient was placed on iodide of potassium, which was rapidly increased up to 1·75 grm. three times a day. It set up acne all over the body, but this contretemps was ignored and the iodide administration persisted in. Within a month the patient was able to walk in his garden, the sinuses were healing, he could swallow food, and the induration over the face and neck was subsiding. Five months after the commencement of the treatment he was quite well, the scars soft, and he had regained flesh. He has been under observation for the past 20 years and has had no recurrence.

d. Facial and cervical actinomycosis is frequently due to infection through the salivary ducts, the mouth and jaw presenting no lesion. The first sign is a nodule in front of the ear or under the jaw. Two important points should be noted, that the nodule is not in the skin but under the superficial fascia, and that there is an early limitation of the movement of the mandible. From this there is extension to the lymphatic glands of the neck and locally an induration involving the skin and fascia. It is important to undertake an exploration at once for the purpose of diagnosis. If this is adopted the objection raised by Gougerot is met; he stated that in France cases of tuberculosis and of staphylococcal infections of the skin had been diagnosed as actinomycosis. Neglected, there may be increasing pain from involvement of the fifth nerve, and a spread to the ear and base of the skull, also from the neck into the chest, or back to the spine.

e. Actinomycosis of the appendix is by far the commonest lesion in the gastro-intestinal tract. The characteristic sign is a deep-seated nodule gradually becoming more and more fixed by a spreading induration. As distinguished from appendicitis in general, there is an absence of acute attacks of pain, an absence of tenderness and of any disturbance of the temperature or pulse. It is most important that the appendix should be removed at once. In an insidious fashion extension occurs backwards to the ilium and spine, rendering the case hopeless; equally so is an extension to the genito-urinary organs of man or woman. As the induration spreads in the ileo-caecal region, the liver and lungs become invaded, whilst dense intraperitoneal adhesions form. Besides the excision of the appendix, any induration should be freely injected at the time of the operation and a course of iodide of potassium continued for a long while. Any induration in the scar of the appendix operation may be caused to disappear by X-ray application and iodine injections. Any tendency to reformation of a sinus should be anticipated.

Actinomycosis in some other part of the intestines may give rise to signs of intestinal obstruction. When this has occurred, there have been also found extensive dense peritoneal thickenings. Possibly the intestinal obstruction may be relieved by an intestinal anastomosis. Beyond this any extensive surgical treatment is out of the question, but the exploration may enable a diagnosis to be made and iodine may be injected into indurations and nodules in the liver, &c. Generally speaking, widespread peritoneal and retroperitoneal indurations and actinomycosis of the liver cannot be cured by iodide of potassium, but the advance of the disease may be delayed.

Kupferberg described a case which furnishes an instance of a neglect of further measures in the case of actinomycotic appendicitis. A soldier aged 22 had the appendix removed, after signs of disease had existed for a month, in November 1916. A sinus formed in the scars, and in February 1917 a small swelling close to the umbilicus was incised and yellow pus let out. A rapidly extending induration of the abdominal wall followed, when a free incision exposed infiltration of the rectus muscle and typical actinomycotic granules were discovered in the pus. At the same time there was found widespread peritoneal thickening. Iodide of potassium supplemented by intravenous injections of salvarsan failed to arrest the disease and the man died in June 1917. There was found *post mortem* an ulceration of the abdominal wall 5 × 4 cm. in diameter, with deep induration and numerous sinuses. The disease had extended backward to the muscles of the loin and to the ilium and right kidney. There was a caecal fistula and metastatic formation in the spleen, liver, and lungs.

f. Pulmonary actinomycosis may be started by inhalation of dust or actual vegetable particles. It also occurs secondarily by extension from the liver through the diaphragm, or by metastases through the pulmonary circulation. It is generally diagnosed only when the disease has penetrated the chest wall. Actinomycotic granules in the sputa is apt to be only a late sign. Possibly an X-ray examination may raise a suspicion of actinomycosis.

The patient has no hectic temperature, but presents opacities to the X-rays towards the bases rather than at the apices. The signs to auscultation and percussion are those of indolent pleural thickening and consolidation towards the base of the lung. If the disease is limited, treatment may be successful. Secondary extension and metastatic lesions may be considered hopeless. Incision, removal of carious ribs, and evacuation of a pleuro-pulmonary abscess must stop short of causing much haemorrhage; some cases have resembled a most vascular sarcoma. Together with this, repeated local injections, X-ray exposures, and prolonged administration of iodide may be followed by a cure.

An extension to the spine sets up the further complication of girdle pains and paraplegia.

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W. G. S.

ANILIN VIOLET IN COPYING PENCILS ACTING AS A SPREADING CAUSTIC, RESEMBLING PHOSPHORUS

When the point of a violet copying pencil has been run into the hand and broken off, the effect is quite different from that following the same accident with the black-lead pencil. The graphite acts simply as a foreign body, and in the absence of any micro-organism becomes encysted until removed, after which the incision made for its removal heals without further complications. When the point of a violet copying pencil is broken off in the hand, the violet dye undergoes solution slowly, the skin at and around the puncture becomes stained violet, and there is a spread of the violet stain in the subcutaneous tissues both in area and depth. This is attended by a persistent subacute inflammation; there is first irritation of nerve twigs causing pain, followed by anaesthesia owing to destruction of nerves. The impacted pencil-point is the centre of a spreading necrosis; shut off from the surface, the point becomes surrounded by a violet-stained débris of necrosed tissue-cells, beyond which is a spreading zone of necrosis, violet in colour. If there is a communication with the surface, the opening of the sinus and the surrounding area is stained violet, and there is a little violet discharge. There is an absence of suppuration because the anilin violet is an antiseptic. If the sinus is laid open, the foreign body is found surrounded by a necrosed débris, and the tissues around, belonging to the subcutaneous tissue and deep fascia, are undergoing necrosis.

Anilin violet contains triphenylmethane, a basic dye, which is mixed with graphite and potter's clay. Both the carbon and the alumina in the two latter are quite harmless, whereas the triphenylmethane can be shown by experiment to have a great affinity for tissue cells. Applied to the cornea or conjunctiva of an animal, the anilin violet causes a local spreading necrosis; if inserted subcutaneously its action is similar to that observed clinically.

Erdheim described, in 1914, two cases of the accident, and he has since met with altogether 23 cases, illustrating the results of the point of a violet copying pencil being run into the finger or hand, &c., and broken off. If the point is impacted in the skin without penetrating to the subcutaneous tissue a dry violet eschar forms, which separates after a week or so.

If the point is broken off in the subcutaneous tissue, but is removed within an hour or so, by an incision sufficient to ensure complete removal, then the incision heals at once without further trouble.

If there is delay beyond an hour or two in removing the foreign body, then the anilin violet begins to dissolve and stain the surrounding tissues. It then becomes necessary to excise the stained tissues surrounding the foreign body in order to arrest the necrosis. If this is not done a subacute inflammation continues. If merely the obvious foreign body is removed, the subacute inflammation goes on, until arrested by a secondary excision of all violet stained necrosing tissue. Failing this, the inflammation and a violet discharge continues for a month or two. The following is a short account of some of Erdheim's cases:

Case 1. A girl of 19 ran the point of the pencil into the dorsum of her foot. A swelling of the foot followed from the toes to the ankle without much pain. The puncture continued to discharge a violet fluid, not pus, for seven weeks, when the point was removed. The incision left a violet-coloured ulcer 3 cm. in diameter, with slightly infiltrated margins, which discharged a violet-coloured fluid. The ulcer was excised three months after the accident, when healing followed.

Case 2. A girl ran the point of a copying pencil into her thumb, which broke off, and a violet discharge followed. A week later the point, 0·5 cm. in length, was cut out, together with 1 cm. of fascia deeply stained violet, and muscle, but leaving some already stained tissue. There followed for the three following weeks a violet discharge from the wound, after which it healed.

Case 3. The pencil in a boy's coat pocket was driven into the subcutaneous tissue of his chest. A week later there was a violet coloured tinge for 1 cm. around the puncture; there had been no pain, nor sign of inflammation. The whole of the stained area around the point of the pencil was excised, and the wound healed by first intention.

Case 4. A student ran the point of a copying pencil into the palm of his hand; the point was removed two days later through a crucial incision. A violet-coloured discharge of connective tissue and fat cells continued for a month; the necrosis involved digital nerves, so that there was loss of sensation in the fingers. The stained area was then excised, including deep fascia, when healing followed.

Case 6. A woman ran the point of a pencil into her finger, and the point, 2 mm. in length, broke off. This was cut out the same day, but a violet discharge followed until the necrosing area was excised, fourteen days after the accident; the healing occurred after a further three weeks.

Case 7. A woman broke off the point of a pencil, 0·5 cm. in length, in the tip of the left index finger. Swelling followed with a violet stained discharge for a month, when all the necrosed tissue was removed by excision and scraping. Healing occurred ten weeks after the puncture.

With the foregoing may be contrasted:

Case 8, in which the point, 0·5 cm. in length, had penetrated the hypothenar eminence. This was removed *within an hour* of the accident, when there had started no necrosis around the fragment, and the incision healed within a week.

Case 13. A recruit accidentally punctured the pulp of the little finger, an incision was made at once, and the fragment removed. It was at the time of the general mobilization in Germany in 1918, and the accident suggested to the man a method of malingering. He repeated the puncturing of his little finger until there ensued a necrosis of the phalanx. In this case there were doubtless complications due to infective micro-organisms. First one and then another bit of the little finger was amputated. Finally, he punctured the stump covering the head of the 5th metacarpal, and on this being excised the pencil end was discovered in the stump. This led to a discovery of the malingering, but the man had meanwhile managed to get himself kept in hospital for three months.

Case 15. A fragment of pencil penetrated the finger, which continued inflamed for ten weeks, until the ungual phalanx had necrosed and formed a sequestrum, in which were violet stainings. Five days after removal the wound showed healthy granulations.

Case 21. The point of a pencil penetrated under the nail of the thumb, which was treated by fomentations for three weeks, when the nail was removed, and the nail-bed scraped. Healing followed.

The microscopic examination of the excised pieces disclosed various stages of necrosis. The peculiar spreading necrosis is set up by the slow solution of the triphenylmethane compound, which appears to act on the tissues much in the same way as particles of phosphorus.

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W. G. S.

ROYAL ... OF ... COLL

ABSTRACTS

NEUROLOGY

Cushing, H. (1). **The major trigeminal neuralgias and their surgical treatment, based on experiences with 332 Gasserian operations. First paper. The varieties of facial neuralgia.** *Am. J. M. Sc.*, 1920, **140**, 157.

Cushing, H. (2). **II. The rôle of deep alcohol injections in the treatment of trigeminal neuralgia.** *J. Am. M. Ass.*, 1920, **75**, 441.

There may be a variety of painful disorders of the nerves supplying the face—disorders which are designated as 'neuralgic'—but which must be clearly distinguished from the more common trigeminal neuralgias. As some of these allied conditions may be exceedingly distressing and may lead the unwary into a needless and futile Gasserian operation, it is well to bear them in mind, so that they may be recognized if possible. Five different types may deserve consideration.

With this preliminary statement, Cushing proceeds to describe the five types in question in this, the first of a series of three papers on the treatment of trigeminal neuralgia.

The neuralgias accredited to the sphenopalatine (Meckel's) ganglion: Sluder's neuralgia. Sluder has drawn attention to the fact that the bony partition separating the accessory nasal sinuses from the sphenomaxillary fossa may be extremely thin or even defective. He believes that inflammatory processes may spread outwards from these spaces and give rise to a congestion of the tissues in the fossa and thus to a neuralgic syndrome from involvement of the sphenopalatine ganglion. The symptom-complex consists of pain at the root of the nose, in the upper jaw and teeth extending backward to the region of the mastoid and causing earache and pain just behind the mastoid process. This may spread to the occiput, shoulder, and pectoral regions. There is also pain in and around the eye. The pain may be constant or paroxysmal.

This form of neuralgia can be differentiated, according to Sluder, by the presence of old or present sinus infection, by its frequent bilateral distribution, and by the absence of facial spasm with the pain.

Cushing does not appear convinced of the existence of a form of neuralgia due to lesion of this ganglion, though the symptom-complex described does occur, is not a true trigeminal neuralgia, and is not relieved by extirpation of the Gasserian ganglion. He gives examples of cases of neuralgia which might possibly have been due to the sphenopalatine ganglion. In one neither removal of the Gasserian nor of Meckel's ganglion gave any relief. In the other two the former operation gave complete freedom from pain.

The post-zoster neuralgias (trigeminal and geniculate). True herpes frequently leaves sequels of a neuralgic type, especially in the middle-aged or elderly. These may be completely incapacitating from their severity and may occur in other than trigeminal herpes.

The neuralgia following trigeminal herpes differs from true tic douloureux in that the pain in the former does not tend to spread into the territory of the other divisions. Moreover, the pain is described as being burning and persistent and unlike the paroxysms of the latter.

The neuralgias accredited to the geniculate ganglion (neuralgia facialis vera; Hunt's neuralgia). Ramsey Hunt has drawn attention to the importance of the sensory root of the seventh nerve apart from its gustatory function. He has collected cases of auricular herpetic affection unquestionably geniculate in origin, some of which have shown neuralgic sequels. Cushing believes that in view of the situation of the geniculate ganglion and its necessarily frequent involvement in middle ear infections, more frequent neuralgias from this cause would be expected were it a true cause. Further, the trigeminal cutaneous field may include the skin area ascribed to the geniculate ganglion and its sensory root, and in many cases of trigeminal neuralgia there may be inaugural pain in the region of the articulatory process of the jaw.

Painful tic convulsive. This, Cushing believes to be an undescribed condition of which he has seen three cases. In it the spasmodic contractions of the facial tic are aggravated by great pain, but the condition should not readily be confused with true trigeminal neuralgia. In the single case in which Cushing removed the Gasserian ganglion there was no relief.

Neuralgias from tumour involvement. Four groups of tumours may give rise to pain of this type; tumours of the cerebello-pontine angle, those involving the ganglion by direct pressure from above, those arising in the temporal bone or pterygoid fossa which press against the ganglion from below, and those arising from the envelopes of the ganglion itself.

In the first type the neuralgias are rare, transient, and not severe; in the few cases of severe pain from this cause on record, removal of the ganglion has been unavailing.

In the second type, in Cushing's experience, neuralgia is rare and not severe, and is generally so overshadowed by the general pressure disturbances as to be a minor symptom. Meningeal endotheliomata most commonly give rise to pain in this way. The ganglion may be grossly deformed by pressure without the production of any discomfort.

Tumours arising in the base of the skull ultimately involve the ganglion, and often give rise to a grinding neuralgic pain from involvement of the ganglion or its roots. Cushing has been induced to perform neurectomy for four such cases from the severity of their pain.

Endothelial tumours arising in the coverings of the ganglion invariably give rise to severe pain. The presence of sensory and motor defect symptoms in the distribution of the fifth nerve distinguishes the condition from true neuralgia. These trigeminal endotheliomata arise, as do the other meningeal endotheliomata, from the arachnoid villi which project into the dura (see *Med. Science*, 1920, **3**, 161), but, unlike the latter, the trigeminal growths remain much longer extradural and their tendency is to erode the cranial base or to pass backward into the posterior fossa, where they simulate an angle tumour.

The minor trigeminal neuralgias. These are multitudinous. They may follow injuries, particularly when nerves have been contused or more seriously damaged. They frequently follow dental procedures, and root infections are also a common cause. Sinus infections by inflammatory involvement of nerves may also give rise to neuralgia. These practically never require alcohol injection or Gasserian removal. 'When some irritative lesion can be found, one can look with equanimity on these local neuralgias, but in the cases in which the initial paroxysm unrelated to any discoverable cause strikes unannounced and others tend to follow, one must realize that these attacks may be the precursors of the major type of neuralgia. It is a matter of importance that this be recognized, if possible, if for no other reason than to spare these unfortunates from the usual sequence of therapeutic procedures, which begin with the extraction of unoffending teeth until all of them may be drawn, with intranasal operations until all the sinuses have been explored, with peripheral neurectomies often repeated, with electrical treatments, violet rays, osteopathy, and drugs without end.' There are minor stages in true major neuralgia, for the disease steadily progresses in its severity and in the extent of involvement of the areas supplied by the three divisions of the nerve.

Early cases with periods of freedom lasting for months at a time, and with the pain largely confined to a single division of the nerve, are classified by Cushing as minor neuralgia. In such cases some temporary measure such as a peripheral neurectomy or an alcohol injection may be resorted to. Major cases are those in which it is obvious that prompt recourse must be had to a Gasserian operation. Cushing thinks that alcohol injections should be confined to the minor neuralgias, or used as an aid to diagnosis in such cases of major neuralgia as may have an obscure symptomatology suggesting a form of pseudo-neuralgia, like one of the five types described above.

Full case records are given illustrating the various forms of neuralgia described in this first part of Cushing's paper.

(2) In the second paper of the series Cushing deals with the employment of deep alcohol injections in the treatment of trigeminal neuralgia. He states that the method has many limitations. The relief is but temporary, and with each successive injection a shorter interval of freedom from pain is apt to be secured. Examples of severe and unsightly complications from misplaced alcohol injections are common in Cushing's experience, and such as rarely follow the Gasserian operation. Among these he enumerates paralysis of the oculomotor nerves, locking of the jaw from infiltration, and subsequent fibrosis of the pterygoid muscles, paralysis of the motor fifth, which may be permanent. Sloughing of the nasal bones and ozoena and severe haemorrhage may follow intranasal injections, and he thinks that there is every reason to decry the nasal injections as practised by the rhinologists. Facial paralysis is also not uncommon. Still more serious are the labyrinthine disorders resulting from injection into the middle ear through the eustachian tube. Cushing states that he never gives an alcohol injection himself without misgivings, and never uses a general anaesthetic for the purpose. With regard to injections into the ganglion itself, as has been advised by some, he speaks even more strongly. He says that any one who is familiar with the appearance of the ganglion in the living, bathed as it is with cerebrospinal fluid, would be terror-stricken at the idea of blindly injecting alcohol into its arachnoid capsule. Its results at best are little better than after extracranial injections, while at worst its complications are more serious than after a bad Gasserian

operation, and in short he protests against it as a dangerous and blind procedure.

On the other hand, he agrees that alcohol injections in careful hands are a blessing to cases of minor neuralgia. However, in major neuralgia it is merely procrastination to use them. With such perfect and permanent results as may be secured by a trigeminal sensory root avulsion, the prolonged and repeated use of alcohol injections should be deplored.

F. M. R. W.

Bostroem, A. Über toxisch bedingte aufsteigende Lähmung mit Hämatoporphyrie. [**Toxic ascending paralysis with haematoporphyrinuria.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1920, **56**, 181.

Bostroem records the case of a woman of 31, who during a lying-in period, developed an illness of indefinite character, which after running a slow course of over two years, terminated suddenly with the appearance of an acute ascending paralysis of Landry type.

During the first and longest phase of the malady she was very depressed, lachrymose, and at times restless and irritable. She complained of vague abdominal pains with paraesthesiae round the lower half of the trunk. During the second year of the illness she became heavily addicted to morphia and such drugs as veronal. From this time abdominal pains and obstinate constipation became a prominent feature. She lost appetite and weight and became anaemic. At no time were there definite signs of any organic nervous lesion. In the spring of 1919—that is, at the beginning of the third year—she had an attack of 'influenza', after which she became rapidly weaker and more emaciated. Late in May of that year definite paresis of the proximal muscles of the lower limbs appeared, followed quickly by that of the upper arm and shoulder muscles. Then the muscles of mastication, deglutition, and respiration became affected, and finally the distal limb muscles. With the muscular involvement, the corresponding jerks became weak and rapidly disappeared and the muscles became hypotonic.

There were no profound sensory changes, but some qualitative alteration of sensation over the regions supplied by the first and second dorsal and the sacral segments. During the last week of this acute ascending paralysis there was retention of urine and intractable constipation. The cerebrospinal fluid was normal. With the onset of the paralytic phase, which lasted for two weeks, there was a remarkable change in the urine, which became port-coloured and contained large amounts of haematoporphyrin.

Although the case in its terminal stage resembled the acute ascending paralysis commonly described as Landry's paralysis, there were certain peculiar features not usually found in that somewhat ill-defined syndrome. Of these the most significant was the haematoporphyrinuria. This condition is most commonly seen in certain forms of poisoning, notably sulphonal poisoning, and rarely with veronal and morphia poisoning.

Bostroem quotes Gunther, who has summarized the literature on haematoporphyrinuria. In the acute forms he found several examples with symptoms referable to the nervous system.

It appears that gastro-intestinal disturbances are the commonest initial symptoms in this condition; abdominal pains, nausea, constipation, while tenesmus and retention of urine are frequent. In a series of 56 acute cases

Gunther found records of ascending paralysis, though the histology showed no constant changes in the nervous system of these cases.

In Bostroem's case the autopsy findings were as follows: The viscera showed no characteristic changes. The naked-eye examination of the nervous system revealed nothing abnormal. Microscopically, the only definite abnormality, and this was extreme, was a marked and very recent degeneration (chromatolysis) of the anterior horn and posterior root ganglion cells of the spinal cord below the level of the upper cervical segments.

Examination by the Marchi method was negative and there was no abnormality of the vessels. The changes were most recent and least intense in the cervical region of the cord. The medulla was normal.

The various causes of haematoporphyrinuria, the different nervous lesions associated with morphia and other similar forms of poisoning, are discussed at great length, and Bostroem concludes that in his case no exogenous poison can be regarded as entirely responsible. He suggests that an intestinal lesion resulting from chronic morphia or other similar drug poisoning may have predisposed to an intestinal auto-intoxication which was the direct cause of the acute ascending paralysis which proved fatal. F. M. R. W.

Brouwer, B. Über Lokalisation innerhalb des Corpus Striatum. [**Localization within the corpus striatum.**] *Deutsche Ztschr. f. Nervenh.*, 1916, **55**, 305.

Brouwer remarks that although physiologists have been accustomed to attribute great importance to the corpus striatum in the matter of heat regulation and similar vegetative functions, the clinico-anatomical studies of the past few years devote little attention to this aspect of the problem, and he records a case of cerebral tumour involving this structure which he considers to throw light upon this side of the function of the corpus striatum. The patient, a man of 39, had suffered from slight urgency of micturition and occasional incontinence for eight years, and also from periodical attacks of speechlessness and flushing without actual loss of consciousness. These symptoms were never severe and he continued at work. For over two years, however, he had himself been aware of progressively failing memory, and for several months before coming under observation he had become increasingly dull, forgetful, and apathetic, so that he had been forced to abandon certain studies and even to give up his work as a machinist. He also complained of constant frontal headache.

Examination a few months before his death, in 1916, revealed an apathetic man entirely devoid of initiative and unable to give a good account of his illness. He spent his day sitting still and silent in bed. His memory was grossly defective. There was double optic neuritis and bilateral defect of smell. The cranial nerves were normal. There was a fine tremor of both hands and sometimes of the lower limbs, but there was absolutely no other defect of the motor system. There were no sensory changes. The tendon-jerks were all present, those on the right side being relatively increased. The cutaneous and plantar reflexes were normal. He passed urine and faeces under him in bed. He failed rapidly and died three days after a lumbar puncture.

Autopsy revealed a glioma in the substance of both frontal lobes, involving the corpus callosum, septum pellucidum, the heads of both caudate nuclei and the putamen, globus pallidus, and internal capsule on the left side.

The tumour partly filled both lateral ventricles. It was only the anterior portions of the corpora striata that were involved. The tumour was the seat of a recent large haemorrhage.

Brouwer attributes the bladder disturbances to the lesion of the anterior portions of the caudate nuclei, and he explains the absence of similar symptoms in the well-known corpus striatum syndromes of C. Vogt and of S. A. K. Wilson on the basis that in these the lesion involved the lenticular nuclei (putamen and globus pallidus) mainly and the caudate nuclei but little or not at all. He then advances the theory that in the lenticular nucleus are localized centres for the control of 'the higher reflex movements' of the voluntary musculature, while in the caudate nucleus reflex activity of the smooth muscles is similarly represented. Hence it is that in lesions of the former we see disturbances of tone and of other aspects of motor co-ordination, while in lesions of the latter, defects of bladder, rectal and even of vasomotor functions result.

There are several objections to this conclusion. In the first place cerebral tumours seldom provide favourable material for physiological observations on cerebral function for reasons that have already been discussed in this very connexion in a recent number of *Medical Science* (1919, **1**, 506). The mental dullness and apathy so common in tumour cases is not infrequently associated with diminished control, or it might be more correct to say with diminished voluntary supervision of the bladder and rectum. More especially is this the case in tumours or other gross lesions of the frontal lobes. It seems probable that in Brouwer's case the growth arose in the frontal lobes and spread backward, and it is therefore not possible to state with certainty that the caudate nuclei were involved eight years previously, when the bladder disturbances first appeared. It seems reasonable to conclude, therefore, that as physiological material the case is quite valueless.

Finally, in the case reported by Economo, and described in this number of *Medical Science,* the caudate nuclei were destroyed at their anterior ends and no sphincter defects are recorded. F. M. R. W.

v. Economo, C. Wilsons Krankheit und das Syndrôme du Corps Strié. [**Wilson's disease and the corpus striatum syndrome.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.* (Orig.), 1918, **43**, 173.

Economo records a rapidly fatal case of progressive lenticular degeneration with hepatic cirrhosis (Wilson's disease) in a boy of 15, in which the predominant symptom was rigidity of the musculature, without any form of involuntary movement such as Wilson found in his cases.

The patient was of healthy stock and normally developed. For two years before his final illness he had had vague symptoms referable to the intestinal system, but of these, though Economo regards them as indicating the seat of the original cause of the malady, there are no details given.

In November 1916 the patient had a spontaneous fracture of one femur, which X-ray examination showed to be atrophic. From this time he was unable to walk properly, but limped and complained of pains in both limbs. When seen by Economo, about six months later, his condition resembled a pseudo-bulbar paralysis with dysarthria, dysphagia, and a fixed rigid face. From this time till his death, in the following June, his condition grew rapidly worse. He became speechless, and, on any attempt to speak, his face was contorted into tonic spasm. He swallowed with difficulty and wept silently and uncontrollably while under examination.

The musculature of the neck, trunk, and limbs was uniformly rigid, the legs, trunk, and neck rigidly extended, and the arms half flexed with the hands in the obstetric position. This rigidity was intense and affected all muscles uniformly. The tendon-jerks were normal, the cutaneous reflexes present, and the plantars flexor. There was no defect of cranial nerves and no sensory defect.

Autopsy revealed chronic pulmonary tuberculosis and tuberculous ulceration of the intestine. There was marked multilobular cirrhosis of the liver and the spleen was enlarged. The brain showed bilaterally symmetrical softening of the lenticular nuclei. The putamen and the adjacent part of the globus pallidus with the head of the caudate nucleus were affected. Their structure was spongy, but there were no large cavities. Microscopically the affected areas showed no evidence of any inflammatory lesion, there was neither perivascular infiltration nor vascular change. Ganglion cells were wanting, and but few medullated fibres remained intact. There was proliferation of vessels and of glia cells.

The process having been of recent origin, Economo was able, by the use of the Marchi method, to trace the fibre connexions of the corpus striatum, and these he describes in detail.

He then reviews the symptomatology of disease of the corpus striatum as recorded in the literature, and concludes from his own case and from others that involuntary movements are no essential component of the syndrome of the corpus striatum, as C. Vogt and Wilson and others have held.

He regards a general tonic spasm, or hypertonus, as the essential feature of pure corpus striatum disease, and with this there is no increase of the tendon reflexes, nor are the other signs of pyramidal tract lesion, notably the extensor plantar response, present.

It is noteworthy that throughout his discussion on rigidity Economo draws no distinction between the rigidity of corpus striatum disease and that characteristic of pyramidal tract lesions. That these differ not alone in the signs that accompany them, but also in their nature and very probably in their origin (vide *Medical Science,* 1919, **1,** 209), would appear to be totally ignored by him, and this undoubtedly detracts from the value of his theoretical observations. F. M. R. W.

Maas, O. Demonstration eines operativ behandelten Falls von angeborenen choreatisch-athetoiden Bewegungen. [**A case of congenital athetosis treated by operation.**] *Neurol. Centralbl.*, 1920, 584.

Inspired by Horsley's description of his treatment of three cases of athetosis by removal of the arm area of the motor cortex, Maas induced Borchardt to treat similarly a case of 'choreatisch-athetoiden' movements of the upper limbs, in which the functional disability of the limbs was but slight. The right motor cortex was exposed, and the arm, hand, and finger areas delimited by electrical stimulation. A strip of cortex about 3 cm. long by 1 broad, and 2 mm. in thickness was excised. The immediate result was weakness of thumb movements and almost complete disappearance of the involuntary movements. Power rapidly returned, as did the involuntary movements. These soon reached the intensity of those in the opposite upper limb. The only sensory change observed was a slight alteration of sensibility to pin-prick on the left hand. There was no tendency to spasticity in the limb.

A case was also shown in which, in 1917, various nerves to the upper limb had been severed for the same purpose. Involuntary movements were still almost entirely absent. F. M. R. W.

Krambach, R. Über einen Fall von Athetose nach peripherer Schussverletzung. [**A case of athetosis following a peripheral gunshot wound.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.* (Orig.), 1920, **53**, 230.

An infantryman was struck in the face by a rifle bullet, which entered at the angle of the nose, penetrated the palate, denture, and tongue, and passed out through the buccal mucosa into the posterior triangle of the neck, making its exit through the upper fossa of the scapula 3½ cm. from the vertebral border. He was said to have lost consciousness for two hours and on recovery found the left arm paralysed, and the left leg somewhat weak.

When examined two months later, in addition to injuries in the direct track of the bullet, there was found wasting of the muscles of the left shoulder girdle and arm. The hand and forearm were cyanosed. Pectoralis, deltoid, the rotators of the shoulder, biceps, triceps, and supinator longus were paralysed. Pronation and supination and finger movements were normal. There was impairment of cutaneous sensibility over the lateral aspect of the limb, and hyperaesthesia over the ulnar half of the wrist and hand. The upper plexus group of muscles showed complete R.D., the lower group partial R.D.

Three months after the injury spontaneous movements began to occur in the affected hand. Examination revealed sensory disturbances in the distribution of the 5th, 6th, and 7th cervical roots and marked athetosis of the left hand. There were no signs of any interruption of conduction in the cord and a diagnosis of haematomyelia or central necrosis in the upper part of the cervical enlargement of the cord was made. The hand movements consisted of slow rhythmic extension, flexion and fanning movements of the thumb, index, and middle fingers. There was fibrillation of the interossei, forearm muscles, biceps, and triceps. The tendon-jerks were brisk. These phenomena were still present two years after the original injury.

F. M. R. W.

Meyer, J. L. The physiologic significance of the Babinski response. *Arch. Neurol. & Psychiat.*, 1920, **4**, 309.

By graphically recording the movements of the various segments of the limb during the progress of a Babinski toe response, and by comparing the tracings so obtained with others representing the movements of the limb in the two phases of normal progression, Meyer concludes that the Babinski toe response represents a phase of the 'stepping reflex', apparently an extensor phase.

Although Meyer quotes the experimental observations of Sherrington and the clinical observations of Walshe and of Riddoch, it is clear that he has not studied them and is not acquainted with the physiological phenomena known to occur in the 'stepping' and 'flexion' reflexes. Thus it has been pointed out that spinal stepping is not elicited by cutaneous stimuli, but only by proprioceptive stimuli, while it was long ago shown by Beevor that the quadriceps extensor femoris is not a physiological entity and that rectus femoris does not act with the vasti. Sherrington confirmed this and found that rectus acted as a flexor in the flexion phase of the stepping and flexion reflexes. Therefore Meyer's method of recording the contractions of rectus and regarding them as indicating knee extension is wholly inaccurate. A study of the graphic records contained in the paper makes it appear very doubtful whether they have the significance Meyer attributes to them, and that he finds simultaneous contraction of agonist and antagonist is probably due to the fact that any large movement of the limb so alters its contours that all his tambours are simultaneously affected.

It seems probable, therefore, that his observations are misleading and his conclusions unwarranted. Moreover, the clinical observations of the writers quoted above have afforded conclusive reasons for regarding the Babinski toe response as analogous with the nociceptive flexion reflex, and have shown that it cannot have the significance of stepping.

Therefore, his conclusions, already known to be incorrect from the observations of the writers quoted above, are based upon untrustworthy data. The writer has studied the graphic recording of the reflex movements of flexion in man in spastic conditions and found air-recording with tambours totally unsuitable and misleading for the reasons given above.

F. M. R. W.

Rodda, F. C. The coagulation time of blood in the new born, with special reference to cerebral haemorrhage. *J. Am. M. Ass.*, 1920, **75**, 452.

Rodda was induced to investigate this question by the fact that in the New Born Clinic of the University of Minnesota post-mortem examinations revealed cerebral haemorrhage in 50 per cent. of all infants dying during delivery or in the first few days of life. In many of these labour was easy and uncomplicated, though breech presentations and premature births were common. Asphyxia neonatorum was not constant and it was also noted that at post-mortem the blood was often quite fluid or but slightly coagulated.

Rodda then reviews the development of our knowledge of the subject, but appears unaware of Spencer's important work (see *Tr. Obst. Soc. Lond.*, 1911, **33**, 203). Among the various views of the causation of haemorrhage he quotes: stretching and tearing of the tentorium from elongation of the skull (Beneke, Seitz); rupture of the superior longitudinal sinus or of the entering veins causing extravasation of blood over the hemispheres (Cushing, Seitz); rupture of vessels of choroid plexuses with blood in the ventricles (Seitz); and finally congestion and engorgement of vessels from obstructed circulation (Cushing).

It is believed that haemorrhage over the convexity of the brain is the usual condition in these cases (Henschen, Seitz, Cushing).

Apart from haemorrhage and death from gross trauma, there remains a class of case in which haemorrhage develops insidiously several days after birth, causing symptoms of compression, convulsions, and death. In these there is usually a large thin unilateral clot over the convexity in the parietal region. There is in these no demonstrable source of bleeding, but examination reveals multiple haemorrhages throughout the body in situations where injury cannot have played a part in their production. More than 25 per cent. of his cases showed these multiple haemorrhages, and this led him to investigate the coagulation time of the blood in the new born. From his studies he concludes that cerebral haemorrhage is common in the newly born and is the most frequent cause of death in the first few days of life. It is not always caused by obstetric procedures and may occur in or after normal labours. The common cause of cerebral haemorrhage is not gross trauma, but mild injury in children with haemorrhagic tendencies, which are manifested by a delayed blood coagulation and bleeding times. This can be controlled by the subcutaneous injection of whole blood in all but the most severe cases, where early surgical interference is called for.

F. M. R. W.

Gunby, P. C. Neuroblastoma sympathicum. Report of one case. *Am. J. M. Sc.*, 1920, **140**, 207.

A report from the Mayo Clinic of the case of a boy of 13 years, who came under observation for failing vision, weakness, and 'small lumps' in the scalp. Another child in the family had 'necroses of the skull'.

There was six months' history of these symptoms, which had been progressive. There had been but little headache and no vomiting. There had been no defect of sphincter control, no haemorrhages or skin rashes, nor any gastro-intestinal or urinary disturbance.

The patient was well-developed but emaciated, with a pale greenish skin. The entire vertex and forehead were nodular with tumours varying from 2 to 6 cms. in diameter. Some were soft, others hard. They were apparently attached to the skull, the sutures of which were separated. The veins of the scalp were greatly dilated. There was moderate bilateral exophthalmos and enlarged hard cervical lymphatic glands. The sternum and ribs were tender to pressure. In the left hypochondrium a large smooth mass was felt. There was bilateral papilloedema, but no signs of focal nervous lesions. The urine was normal. X-ray of the skull revealed a diffuse porosity resembling the osteoclastic type of bone malignancy. A provisional diagnosis of neuroblastoma sympathicum, probably primary in the left suprarenal, was made. The child died in two months.

Post-mortem examination revealed 'large malignant hypernephroma (?) of the left adrenal; multiple extensive hypernephroma (?), metastases to the bones of the skull, sternum, ribs, and to the lateral lumbar and retro-aortic lymph nodes; very extensive tumour rarefaction and softening of the skull bones, with very extensive tumour moulding of the brain. The spleen was considerably enlarged.

None of the features of hypernephroma proper were found in the adrenal on microscopic examination. The diagnosis of neuroblastoma was thus confirmed.

F. M. R. W.

White, F. W. A brief experience with appendicostomy and cecostomy for intestinal stasis in epilepsy and neurasthenia. *Am. J. M. Sc.*, 1920, **140**, 199.

The paper relates to four cases, two of epilepsy and two diagnosed as neurasthenia, in which there was a considerable degree of intestinal stasis, and in which appendicostomy or cecostomy was performed with subsequent lavage of the large intestine for periods of from six to twenty-six months. The hypothesis underlying this treatment was that stasis of the contents of the colon led to absorption of some toxic material, which was responsible for the symptoms, and that this could be prevented by keeping the bowel cleaned out.

The two cases of epilepsy were both of fourteen years' duration. The two other cases had 'pronounced chronic neurasthenic symptoms, headaches, insomnia, indigestion, anorexia, loss of weight, poor circulation, mental apathy', &c.

The necessity of carefully selecting cases for this treatment is emphasized and the indiscriminate use of surgery for such conditions is condemned.

Speaking of his results, White says that the actual results of the operation and subsequent lavage are difficult to judge in this class of patient. The immediate results were not striking, in fact one neurasthenic was definitely worse for some months. The late results have been no more favourable. Both neurasthenics 'felt' benefited, one was slightly so. The epileptics, one of whom had also chronic nephritis, had a complete cessation of attacks after operation, for two months in one case and for eight in the other. However, eighteen months later both were in the same condition as before operation. White would hesitate to advise operation again in similar cases. F. M. R. W.

Netter, A. Origine commune de la varicelle et d'un certain nombre de zonas. [**The common origin of chicken-pox and of some cases of herpes zoster.**] *Bull. Acad. de méd.*, 1920, 3e sér., **83**, 588.

Although expressing himself as already convinced of the common origin of chicken-pox and herpes zoster, by the observations of Bokay and of writers in this country, it is only recently that Netter has been able to satisfy himself of this identity of cause by two personally observed cases.

He gives a complete bibliography with essential clinical details of the total number of recorded associations of these two conditions. With his own examples there are 69 in all. In 59 of these chicken-pox followed herpes, in 10 the order was reversed.

Netter's first observation consisted in the appearance of a case of herpes in a child, 15 days after exposure to infection in a chicken-pox ward. His second was that of a child admitted to hospital with lethargic encephalitis and herpes from a boarding school in which there were 15 cases of chicken-pox. The incubation period here was 14 days.

He then quotes two similar cases recorded by Feer (*Schweiz. med. Wchnschr.*, 1920, Jan.). Here also the incubation period was 14 days.

He concludes that chicken-pox and herpes zoster (in some instances) are due to the action of the same virus, and that in the latter disease the virus acts upon the posterior root ganglia. In further support of this view he quotes 16 recorded cases in which both affections were present in the same patient. F. M. R. W.

Marie, P., et **Mlle Lévy.** Le syndrôme Parkinsonien dans l'encéphalite. [**The Parkinsonian syndrome in lethargic encephalitis.**] *Bull. Acad. de méd.*, 1920, 3e sér., **83**, 539.

Marie holds that paralysis agitans and the Parkinsonian syndrome of certain cases of lethargic encephalitis differ essentially, not alone in their clinical characters, but also in the underlying lesions in each case. He discusses in detail the clinical points of difference between the symptomatic and the true paralysis agitans.

(1) Age of onset. While paralysis agitans is rare before 45 years of age, the encephalitic syndrome is commonest in the third and fourth decades of life, and may even occur in infancy.

(2) The signs of a general toxi-infection and of certain cranial nerve palsies and lethargy are only found in encephalitis and not in paralysis agitans.

(3) The mode of onset differs widely in the two cases. In paralysis agitans it is slowly progressive and hemiplegic in onset. In encephalitis it appears suddenly and to its full extent.

(4) In encephalitis the typical tremor of paralysis agitans is wanting. In the rare cases of this form that show tremor, this is not of the true paralysis agitans variety, but appears with or is increased by voluntary movement, which is the reverse of what happens in paralysis agitans.

(5) In paralysis agitans defective movement of the tongue is rare. In encephalitis there is frequently a difficulty in protruding it, while it often shows tremor or fibrillary twitchings.

(6) In encephalitis there may be difficulty in opening the mouth, and mastication is carried on by the incisors alone and not as normally with the molars.

(7) The course of the symptoms is widely different in the two diseases.

F. M. R. W.

Boas, K. Über alternierende Fazialislähmungen. [**Alternating facial paralysis.**] *Neurol. Centralbl.*, 1920, 367.

Relapsing or recurrent facial paralysis is relatively rare. Bernhardt collected a series of 60 cases from the literature (1899), of which 66 per cent. had recurred once and 31 per cent. twice. In all the literature there are to be found only three examples of a third recurrence and a single case of a fourth.

Boas records a case with three recurrences at long intervals (1906, 1913, 1920) in a man of 30 at the date of examination (1920). On the first occasion and following extensive teeth extraction the right face was paralysed; eight days later the opposite side was similarly affected. Both sides recovered completely in eight weeks.

On the second occasion the right face was again suddenly paralysed, recovering within two months.

In April 1920—in the spring, as on the previous occasions—the patient awoke one morning with a complete left facial palsy. At this time there were revolutionary disturbances in Leipzig, and in addition to this possible psychological factor there was a history of exposure to cold. Four weeks later recovery was progressing favourably. There was no reaction of degeneration in the affected muscles, but a definite hypo-excitability to both interrupted and continuous currents.

Of pure recurrent facial palsy Boas distinguishes two types, a first in which the recurrences are all on the same side, and a second or alternating type in which the two halves of the face are affected alternately. His case belongs to the latter and more common type, though he would distinguish it still further as recurrent facial diplegia.

F. M. R. W.

Henneberg. Über Salvarsan-Hirntod. [**Fatal brain lesions from salvarsan.**] *Neurol. Centralbl.*, 1920, 585.

Death occurred in three patients following a series of neosalvarsan injections in the usual doses and at proper intervals. No signs of cerebral syphilis were found in any of the brains.

Case I. A condition of brain purpura or encephalitis haemorrhagica was found. There were numerous petechial haemorrhages scattered throughout the hemispheres and the corpus callosum and in the internal capsules, intense congestion of the choroid plexuses, and recent thromboses in the choroid veins. There were also numerous small areas of hyaline necrosis with ring haemorrhages.

Case II. A similar condition to that described in Case I, but of somewhat different distribution. There were symmetrical areas, of the bulk of a cherry stone, of extravasation of the blood in the thalami, and larger lesions in the pons. The choroid plexuses were normal. The kidneys were intact in both these cases.

Case III. A woman of 48 with bronchiectasis but no syphilis. Coma and death followed an injection of ·45 grs. Pontine haemorrhages and infarcts were found. There was old renal and arterial disease.

The lesions in the first two cases are in no way specific, but are found in other forms of poisoning. It appears that salvarsan leads to venous stasis in dilated vessels, thence to thrombosis and extravasation of blood. The great vein of Galen seems specially liable to be affected in this way.

F. M. R. W.

Kisch, B. Reflexus cochleopalpebralis und Ohr-Lidschlag-Reflex. [**The cochleopalpebral reflex and the ear-eyelid reflex.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 149.

The author insists that the reflex described by him under the latter title in 1918 is distinct from the reflex described by v. Bechterew, though Galant considers them identical. (The Ear- Eyelid Reflex consists of reflex blinking, often with unilateral secretion of tears, when the external auditory meatus or membrana tympani are stimulated mechanically or thermally. It is never absent in normal subjects.)

C. L. E.

Ebbecke, U. Chronische Narkosewirkung und rhythmische Reflexe. [**Chronic narcosis and rhythmic reflexes.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 73.

A shock-like condition of lowered tone of the spinal centres is the common result of the removal of the control of the higher centres, and this is seen in the temporary loss of higher control under the influence of alcohol or other narcotics. After repeated narcotization with ether (which induced chronic changes in the higher centres), however, the lower centres in a cat showed greater independence under the influence of general narcosis. Definite and persistent rhythmic movements were now seen under the influence of the narcotic: these were movements of progression, and the method of graded narcosis allowed an analysis of these reflexes to be made. Cooling of the body-surface increased the reflex movements, as a result of contributory skin reflexes, but a fall of body temperature brought about inhibition. The acquisition of independence of higher control on the part of the lower centres also applies to medullary centres and lower cortical centres.

C. L. E.

PATHOLOGY AND BACTERIOLOGY

Bordet, Jules. Traité de l'immunité dans les maladies infectieuses. [**Treatise on immunity in infectious diseases.**] Paris, 1920, Masson, 720 pp., price 40 francs.

In the short space at our disposal it is impossible adequately to present any but a cursory notice of this masterly work by the great Belgian bacteriologist, Jules Bordet. Through a long series of years he has been known by first-class discoveries, particularly in the domain of immunity, and with a rare prevision has been largely responsible for piloting the subject into the channels in which it is being studied with most success at the present day. Largely through his work, immunity is no longer a narrow subject dealing with the prevention or recovery from infective disease, but has become a great biological problem with branches extending into practical human medicine, physiology, and the basic biological sciences. It is with this larger problem that Bordet has now attempted to deal, and, in a large measure, with the success of one who is familiar with every aspect of the science, who has lived through the whole of the immunity period in medicine, and has contributed much to its advancement, who has a broad philosophical outlook, who is a clear exponent of difficulties, and who is still a young man in his prime.

From the days when Pasteur and Chauveau attempted to explain the observed facts of insusceptibility to *rouget*, chicken cholera, and anthrax, the immunity doctrine has passed through various crises, which for a time have dominated all lines of research. Thus we have the great phagocytic era founded and defended with extraordinary skill by Metchnikoff and a host of his pupils. Following this we have the humoral doctrine of Hans Buchner, v. Behring, Ehrlich, R. Pfeiffer, and the Teutonic school in general, with a vast and almost unmanageable literature. To this succeeded the doctrine, which may be called cellulo-humoral, inaugurated by Denys and his fellow workers of Louvain from 1894 onwards. Then came a period of great activity in which numerous facts were accumulated on the origin of protective substances, and on the union of antigens and antibodies. The knowledge thus acquired demanded a revision of the theories and there thus set in a new crisis—the physico-chemical—which was associated with the names of Arrhenius and Madsen. The foundations of a new subject—immuno-chemistry—were laid.

Bordet was early in the field during the phagocytic epoch, and since then has with astonishing diligence and ability worked in the most diverse directions, clearing up difficulties here, discovering new principles there, with a success which has compelled admiration everywhere, and has made him the foremost bacteriologist and immunologist of the age.

This great treatise sums up his views, based on his own unique practical experience and his extensive knowledge of the work of others. It cannot be doubted that this book will remain a standard for years, and must rank as a highly important contribution to the medical literature of the twentieth century. It is not an ordinary text-book, it is not a book for examinations, but it will have to be read and pondered by all those who have an interest in the wider medicine that is everywhere being built up to-day on the foundations of chemistry, biology, physiology, and pathology.

The treatise is divided into four main parts. In the first is considered the problem in general, six chapters being included for the discussion of infection, natural immunity, acquired immunity, active and passive immunity, the induction of immunity, allergy, and immuno-therapy. The second part is a masterly account of cellular immunity and the mechanism and significance of phagocytosis. In the third part the facts of humoral immunity are analysed, with discussion of the antitoxic, agglutinating, precipitating, lytic, and opsonic antibodies. Long chapters are devoted to the fixation of alexin—Bordet's own discovery—the antigen-antibody complex, and the mechanism of anaphylaxis. The last section is a well thought out analysis of the problem of the reaction of the organism as a whole, with a special chapter on immunity in different forms of disease.

There is no detailed bibliography to which the reader may refer for further knowledge, there are no illustrations or schematic representations. It may be doubted whether the author visualizes things in such a way. Like most French books, there is also no index. It is, however, a genuine treat to read such a work, for the author, like most people who write in French, has an extraordinarily easy and uninvolved style, with a fresh, simple, and original way of expressing himself. Even when the subject is inherently involved the author conveys the impression that he understands it thoroughly. All the knowledge is apparently up to date and the book must have been written during the war. This is all the more remarkable as the author must have lived in very unpropitious circumstances in Brussels.

W. B.

György, P. Beitrag zur Systematik der Paracoli-Bazillen. [**A contribution to the study of paracolon bacilli.**]. *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1920, Orig. **84**, 321.

The term 'paracolon bacillus' was given long ago by Gilbert to certain coli-like bacteria which differ from true *B. coli* in being unable to ferment lactose or to coagulate milk. Later it was found that there were variations in motility and in the power to produce indol. The concept however of 'paracolon' bacilli has, however, been very indefinite, and more refined methods of diagnosis have served to separate off new species which may or may not have a pathogenic action. The present author has made an exhaustive study of 47 strains of non-motile paracolon bacilli isolated from the stools of patients suffering from typhoid, paratyphoid, or dysentery, or from convalescents who had recently had these diseases. He compared these strains with five others which were motile. Very exact comparisons were made of the morphological, biochemical, and serological reactions, with the result that he was able to differentiate a number of groups which would clearly indicate that the paracolon bacillus is not an entity in any sense of the word. He differentiates 22 types alone with regard to colony formation. More than half of the strains were pathogenic for mice. An exhaustive bibliography accompanies the paper, which also contains interesting observations on the 'mutation' in several of the groups.

W. B.

Herrnheiser, G. Paratyphusbacteriurie. [**Paratyphoid bacteriuria.**] *Med. Klin.*, 1920, **16**, 469.

There is a general paper based on the examination of 72 cases of bacteriuria due to Paratyphoid A and 85 cases due to Paratyphoid B. The incidence of urinary infection in the two diseases is estimated at 40 per cent. The passage of bacteria may be ephemeral, continuous, or intermittent, and usually begins in the second to the fourth week or even later. In long-standing cases of bacteriuria due to *B. paratyphosus A* or *B* an actual cystitis may be set up with ulceration. In all cases of ureteral catheterization it was found that the upper passages were involved in the infection. Five cases died during the bacteriuric period, and all showed focal changes in the kidney on post-mortem examination. In the majority of cases the urinary infection must be regarded as a descending one, although an ascending infection from the urethra is possible. W. B.

Perry, H. M. The antigenic properties of *B. psittacosis*. *Brit. J. Exper. Path.*, 1920, **1**, 131.

In 1892 an epidemic disease, known as psittacosis, was observed in France in a consignment of parrots, and human beings became infected by contact with these birds. The human disease had many features in common with typhoid. Nocard isolated from the birds a bacillus which he called *B. psittacosis*, and later, in another outbreak, Gilbert and Fournier found the same organism in human cases.

The present author also isolated a bacillus from a case of enteritis in a parrot, which he shows to have identical serological and other characters to the original strain of Nocard, a culture of which he obtained. Further, his strain has the same reactions as *B. aertrycke* (' Mutton ' variety).

P. F.

Torrey, J. C., and **Rahe, A. H. An experimental study of the effect of autogenous *B. coli* vaccines on the intestinal colon bacilli of dogs.** *J. Immunol.*, 1920, **5**, 133.

This research was carried out to determine whether there is an experimental basis for the use of autogenous vaccines of *B. coli* in the treatment of such conditions as chronic intestinal toxaemia and eczema, the assumption being that toxic products giving rise to these conditions are produced through the activity of strains of *B. coli* vegetating in the gut, and these strains may be suppressed or eliminated by specific immunization. Normal dogs were used in the experiments, and were kept on a constant diet of boiled rice and ox-heart, a diet which had already been shown by Torrey to be favourable for the development of an intestinal flora dominated by *B. coli*. This flora was at first carefully studied for a period of four to six weeks on Endo plates containing saccharose, and a definite group of saccharose-fermenting coli micro-organisms was selected for the test. With these selected cultures a vaccine was prepared for the dogs, and in addition rabbits were inoculated for the production of a specific antiserum. The dogs having received repeated doses of the vaccine, the result was controlled by the estimation of the number of saccharose-fermenting coli bacteria in the faeces. Although considerable differences obtained in the case of different dogs, the author considered that it was established that the autogenous vaccine had produced at least a temporary suppression of homologous bacteria vegetating, naturally, in the intestine. The doses of the vaccine had to be large to produce this result. Cultural results indicating a decrease in numbers of the type of *B. coli* in question were associated with a coincident rise of specific antibody in the blood. In order to witness the effect of the vaccine a uniform diet must be obtained. W. B.

MATSUMOTO, M. A study of different methods for the preparation of *B. typhosus* antigen. *J. Immunol.*, 1920, **5**, 111.

This is a study of the effects on the complement-fixation test of different methods of preparing typhoid antigen. The antigens all came from the same strain of *B. typhosus*, and it was found that various methods of preparation cause very distinct differences in antigenic sensitiveness, when tested in complement-fixation experiments against the serum of rabbits immunized with the homologous *B. typhosus* in the presence of an anti-sheep haemolytic system. Nine separate antigens were prepared, and one of the simplest —a 14-day-old broth culture heated at 60° C. for one hour and preserved with 0·5 per cent. phenol—gave uniformly the best results. An antigen composed of living typhoid bacilli, suspended in physiological saline solution and freshly prepared as required, followed it closely in efficacy. Antigens prepared by suspending the powder of dried and ground bacilli in saline solution proved next best in point of sensitivity. The poorest antigen was one prepared from the filtrate of bacilli autolysed in distilled water, the filtrate being subsequently heated at 56° C. for one hour on three successive days, after which it was preserved in the refrigerator in the presence of 0·5 per cent. phenol. The anticomplementary activity of the various antigens did not appear to differ markedly the one from the other. Several were more haemolytic than the others and all were durable over a period of six weeks. The author considers it probable that antigens containing the whole microbe, living or dead and suspended in saline, will be found to be the most useful in infections other than typhoid. W. B.

SANDS, J. E. A comparative study of methods for the preparation of typhoid agglutinogens. *J. Immunol.*, 1920, **5**, 97.

This is a study of the influence of the mode of preparation upon the qualities of typhoid agglutinogen with particular reference to the influence of heat and the kind, and more particularly the concentration, of chemical germicide or preservative employed. The same culture of *B. typhosus* was used throughout and had long been employed in agglutination tests. It was sensitive to agglutinins and usually free from spontaneous clumping. Twenty-one different suspensions were made, six being prepared from a 96-hour culture in plain neutral broth. Three of these were heated to 60° and two then received the addition of phenol or phenol and glycerine. Three were unheated, but to one was added 0·5 per cent. phenol, to another 0·5 per cent. tricresol, while the third received 1 : 2,000 mercurophen. Ten antigens were prepared from cultures grown on plain neutral agar, the resulting bacterial mass being suspended in saline solution to which were afterwards added formalin (in concentrations from 0·1 per cent to 5 per cent.), phenol (in concentrations of 1 per cent. and 5 per cent.), or mercurophen (1 : 1,000 to 1 : 5,000). The remaining five emulsions were prepared by suspending unheated cultures from agar in concentrations of sodium chloride varying from 0·85 per cent. to 5 per cent. A macroscopic test was employed, all tubes being incubated at 55° C. for about 24 hours, the results being then read — usually by two observers. Each emulsion was tested with five immune sera. The results were recorded according to the maximum dilution of each serum in which agglutination was detectable by the naked eye, viz. the production of flocculi with or without some sediment. Five charts are presented to show that the mode of preparation of the antigen has a profound effect upon the results of agglutination tests.

The density of the suspension was found to have an important influence regardless of the method of preparation. Suspensions, in saline solution, from agar cultures were generally superior to broth cultures. Distilled water alone was an unsatisfactory menstruum for the suspension of typhoid bacilli. Heating the cultures at 60° C. for two hours generally increased the sensitivity to the specific agglutinins. The best emulsions were found to be those containing 1 to 2 per cent. of formalin, being superior to emulsions of similar opacity suspended in phenol, tricresol, mercurophen, and glycerine. Contrary to the experience of Dreyer, the author considers that the best typhoid emulsions are made from growths on agar for 48 hours, after which they are suspended in chemically pure sodium chloride shaken with beads, diluted to a density representing about 2,000 million bacteria per c.c. Finally, neutral formalin is added to the amount of 1 per cent. W. B.

Miura, Y. Experimental study of the sensitized cholera antigen. *J. Immunol.* 1920, **5**, 145.

The author has compared the agglutinating and bacteriolytic titres of the serum of rabbits or human beings inoculated with one or other of two sensitized cholera vaccines. The one was prepared in the usual (wet) way the other being obtained as a powder dried over calcium chloride, as it had been found that sensitized vaccine in solution has not good keeping qualities. It was found that the sensitized powder is nearly equal in its antigenic properties to the ordinary sensitized vaccine kept wet throughout. In human beings the clinical symptoms, following the injection of sensitized cholera vaccine powder, were limited to slight lassitude or headache. For the most part febrile reaction was absent. W. B.

Rosenow, E. C. Studies in influenza and pneumonia. V. Observations on the bacteriology and certain clinical features of influenza and influenzal pneumonia. *J. Infect. Dis.*, 1920, **26**, 469. **VI. The leucocytic reaction in influenza and influenzal pneumonia.** *Ibid.*, 1920, **26**, 492. **VII. A study of the effects following the injection of bacteria found in influenza, in normal throats, in simple nasopharyngitis and in lobar pneumonia.** *Ibid.*, 1920, **26**, 504. **VIII. Experiments on the aetiology of 'gastro-intestinal' influenza.** *Ibid.*, 1920, **26**, 557. **IX. Changes in the green-producing streptococcus induced by successive animal passage and their significance in epidemic influenza.** *Ibid.*, 1920, **26**, 567. **X. The immunologic properties of the green-producing streptococci from influenza.** *Ibid.*, 1920, **26**, 597. **XI. Therapeutic effects of a monovalent antistreptococcus serum in influenza and influenzal pneumonia.** *Ibid.*, 1920, **26**, 614.

The author refers to the frequent occurrence of microbes of the pneumococcus-streptococcus group in all epidemics of influenza from the

1889/90 pandemic onwards. In the investigation of these microbes he was struck with the marked changes which they undergo, both in infective and immunological properties, giving rise to variants or mutants. From these observations he concluded that there was a possibility that the protean clinical characters of 'influenza' over wide areas might be explained on the assumption that variants of microbes normally found in the respiratory tract had developed under some influence. He had the opportunity of studying the question thoroughly in the course of four epidemic waves of influenza which swept over Rochester, Minn. Cultures were made from the respiratory tract and blood during life and after death, the medium used being mainly a 'vitamine' blood agar. On this, green-producing streptococci (including pneumococci) were found more constantly and in larger numbers than any other micro-organisms. Thus, in material from 571 cases, green-producing streptococci were isolated from sputum in predominating numbers or in pure culture in 41 per cent., and not in predominating cultures in 54 per cent., a total of 95 per cent. They were isolated from the pulmonic exudate in large numbers or pure culture in 18 per cent., and in smaller numbers in 37 per cent., a total of 55 per cent. of the 107 cases that came to autopsy. Haemolytic streptococci occurred in the sputum as the dominant microbes in 9 per cent., and as subsidiary microbes in 29 per cent., a total of 38 per cent. of the cases examined during life, and they occurred in the pulmonic exudate in predominating numbers in 23 per cent., and in subsidiary numbers in 54 per cent., a total of 77 per cent. of the cases examined *post mortem*. Staphylococci were isolated from the sputum in 72 per cent. of the cases, and from the lungs after death in 50 per cent. *B. influenzae* was isolated from the sputum in 13 per cent., and in predominating numbers in 5 per cent. In the 5 per cent. of cases in which it was isolated after death it was never the chief organism in point of numbers. *M. catarrhalis* and *B. mucosus* were found in the sputum in the proportions of 6 per cent. and 1·8 per cent. respectively, and in the pulmonic exudate to the extent of 3 per cent. and 11 per cent. respectively. The author observed that marked variations in the type of flora occurred at different stages of the disease and at different periods of the epidemic wave, a tendency being displayed of replacement of the green-producing streptococci by those of a haemolytic type. A large number of cultures of green-producing cocci were submitted to fermentation tests, when considerable differences were observed, and it was noted that those that fermented raffinose, mannitol, salicin, and inulin tended to lose this property after six to nine months in artificial culture. The author is convinced that in the majority of cases of influenza studied by him *B. influenzae* played little or no part in the production of the symptoms. He also believes that the 'diplo-streptococcus' of English writers, *Diplococcus epidemicus* of Bernhardt, *Diplococcus mucosus* of Stephan, and the pleomorphic streptococcus of Wiesner, in Vienna, are identical with the green-producing streptococcus or modifications thereof. He further considers that the mutations of this microbe observed *in vitro* indicate that the changes in bacterial flora at different stages of the disease in the individual and in the epidemic waves may not be the result of mixed or secondary infections as is generally believed.

In the second paper the author has made a study of the leucocytic reaction in human cases of influenza and in guinea-pigs inoculated with green-producing or haemolytic cultures obtained from human cases. From a large number of observations it is now known that leukopenia is an important aid in the diagnosis of influenza, but its nature is the subject of discussion. The prevailing idea would appear to be that some unknown virus produces the initial diminution in the leucocytic count and interferes with the secondary leucocytosis which might be expected to occur from the streptococci or pneumococci met at a later stage of the disease. The present author does not agree with this conception and considers that the absence of leucocytosis may be the result of invasion of streptococci alone. These cocci, according to him, produce, both *in vivo* and *in vitro*, soluble, filterable substances, the intratracheal injection of which determines, in guinea-pigs, a sharp reduction in the leucocytic count. The author's third paper, illustrated by eight plates, is concerned with the effects following the injection, in diverse ways into animals, of material obtained from influenzal and other cases, some of which were normal persons. In particular, intratracheal inoculations were practised in guinea-pigs. From a large number of observations the author classifies the results in four groups. In Group I the symptoms produced were slight and consisted of malaise, loss of weight, moderate leukopenia, with slight or moderately increased respiratory frequence followed by recovery, after which the animals were found to be immune to injections of heterologous strains. In Group II all the symptoms were more pronounced and dyspnoea was often very marked, death often taking place in one or two days with anaphylactic symptoms, voluminous lungs, and broncho-pneumonia, with or without abscess formation. In Group III the symptoms were very severe from the start, and progressed without intermission till *exitus*, which occurred in two or three days from increasing cyanosis and anaphylactoid symptoms during which haemorrhagic oedematous fluid escaped from the nose in a number of instances. The autopsy revealed huge lungs and extensive consolidation very similar to that seen in so many fatal cases of influenza in man. In Group IV extreme dyspnoea followed almost immediately on the injection of cultures or filtrates, and many of the animals died while making violent efforts to breathe as a bloody fluid ran from the nose and mouth. The lungs were huge, haemorrhagic, and oedematous throughout. Experiments showed that green-producing cocci may be so small that they traverse filters, and that filtrates obtained may be infective and cause death.

When control strains of streptococci and allied micro-organisms were injected by way of the trachea the results were very different from those described above, and the mortality was much lower. In conclusion, the author believes that he has been able, by intratracheal injection of green-producing streptococci from influenza in man, to reproduce completely the clinical and pathological picture of the human disease.

In his fourth paper Rosenau deals with the vague conception of 'gastric influenza' which has been described so frequently in the last as also in former pandemics of the disease. From the stools of a number of cases he isolated green-producing streptococci, and he particularly details the results of the examination of material from a boy, aged 3, who died after suffering from acute 'gastric influenza' for six days, and from his sister, aged 15 months, who had the disease but recovered. Injections of freshly isolated 'green' streptococci, from these two cases, into 14 guinea-pigs produced well-marked lesions in the gastro-intestinal tract in 12. A strain which produced pancreatitis in a guinea-pig in the second passage produced the same condition in the guinea-pig, rat, and dog on intravenous injection in the third passage. The property, however, disappeared in the fourth passage.

In the fifth paper the author has made a study of the effects of the passage of green-producing streptococci, isolated from influenzal cases, through the lungs of guinea-pigs, and he finds that there is an exaltation of the virus for one or two passages after which the virulence diminishes. Cyanosis and leukopenia and death from a haemorrhagic oedematous distension of the lungs are the characteristics of the virulent virus. In later passages by intratracheal inoculation when the virus becomes attenuated the dyspnoea and leukopenia are less marked. Evidence is adduced to show that green-producing streptococci may acquire haemolysing powers, and conversely that haemolytic cocci may pass into the green-producing type. Some general remarks on the variations in the bacterial flora at successive stages of influenzal epidemics are introduced to support the above views of the mutation of microbes in the body.

The sixth paper contains the author's results on the immunological reactions evoked by green-producing streptococci, isolated from cases of influenza, when injected into the horse.

The conclusion was reached that green-producing streptococci isolated early in epidemic waves are, agglutinogenically, homogeneous. After cultivation on artificial media, and after repeated animal passages, as well as late in influenza and influenzal pneumonia, the strains tend to become heterogeneous.

The seventh and last paper of the series briefly records the results in the treatment of 12 influenzal patients with the serum prepared from one strain of green-producing streptococcus. At the same time, observations were undertaken on the immune reactions of streptococci isolated from the patients treated serotherapeutically. With one exception, all the 12 patients were seriously ill. Five recovered and seven died. Three patients were actually moribund when the treatment was initiated. Specific agglutinating properties in the patient's serum were noted in all cases where the antiserum manifested its action therapeutically. W. B.

Fildes, P., and **McIntosh, J.** **The aetiology of influenza.** *Brit. J. Exper. Path.*, 1920, **1**, 159.

The first instalment of this review (*vide* this Journal, 1920, **2**, 482) consists of a recapitulation of the criteria which should be fulfilled by a supposed pathogenic virus before it can be accepted as the cause of a particular disease. These criteria are brought forward as modernized 'Koch's postulates' and are summarized as follows:

1. The virus should be capable of being recognized in a large proportion of the cases of the disease, preferably in relation to the chief lesions.
2. The virus should be shown to be living.
3. The virus should be capable of reproducing the disease in other animals.

In the present (final) instalment, the claims of two varieties of virus, each of which has been described as the cause of influenza, are tested by the criteria set up.

Firstly, the filter-passing viruses of Kruse, Nicolle and Lebailly, Gibson, Bowman and Connor, and many others are reviewed. It is held that these supposed viruses are not capable of being recognized in that they are indistinguishable from bodies which are found in normal tissues.

It is also held that there is no evidence of life in the bodies described. The alleged cultivations in series are due to well-known inanimate particles which are common in the type of culture used.

The demonstration of pathogenic effect of such cultures is attributed to faults of technique or to toxic substances which have no relation to influenza. The results of experiments upon animals are not characteristic of influenza and the experiments are often entirely uncontrolled. The alleged positive results upon man were usually obtained when influenza was rife, and are thus inadmissible or are clinically unsatisfactory.

It is pointed out that Lister and Taylor, McIntosh, and others, in experiments not subject to these objections, obtained negative results with filtered viruses. Thus this class of supposed virus fails to justify itself.

B. influenzae of Pfeiffer is then discussed according to the same principles. It is held that the infrequency with which German and other authors have found this bacillus is due to the use of inferior media, as shown by the high percentage of positive results obtained by Matthews, Eyre and Lowe, Fildes, Baker and Thompson, Martin, Schorer, McIntosh, and others in the sputum. Further, Patterson, Little and Williams, Muir and Wilson, Lister, Olsen, and many others have found the bacillus *post mortem* in many cases, and in close relationship to the chief lesions. Many authors have also described *B. influenzae* in normal persons or in non-influenzal diseases, but this does not detract from its claim to be the cause of influenza.

The second criterion, the life of the virus, is not in dispute, but the question of the reproduction of influenza with cultures presents great difficulty.

It may be assumed that *B. influenzae* is capable of infecting man because of the presence of specific antibodies in the blood of many cases, but it cannot be argued from this that the disease produced is influenza. Direct efforts to reproduce influenza in man with cultures of *B. influenzae* have failed (Lister and Taylor, Rosenau, &c.).

In animals the effect of massive doses of *B. influenzae* in saline suspension is trivial; on the other hand, liquid cultures of specially selected strains are constantly pathogenic to guinea-pigs or rabbits. Introduced into the peritoneal cavity, however, they exhibit no constant effect upon the lungs. Blake and Cecil, by using specially prepared strains and introducing these directly into the trachea of monkeys, frequently produced a capillary bronchitis and pneumonia and accompanying complications. These lesions were due to *B. influenzae* alone, and bore a very close resemblance to those of influenza. The same cultures when inoculated into the noses of monkeys produced an affection clinically resembling an uncomplicated influenza, while in some cases the typical pneumonia developed twenty-four hours later.

The essential toxicity of the liquid cultures is due to a bacterial toxin (Parker and others). An antitoxin can be prepared which shows a certain slight degree of protective action. The intravenous injection of this toxin into guinea-pigs or rabbits constantly produces a series of lesions chiefly affecting the lung. These lesions are shown to bear a close resemblance to what are considered to be the essential lesions of influenza.

A comparison between a supposed experimental influenza and influenza in man is, however, uncertain because of a doubt as to what are the fundamental lesions of this disease. The authors, however, conclude that, subject to this uncertainty, the lesions produced in animals by *B. influenzae* are the same as the lesions of influenza in man, and the final criterion of reproduction of the disease is thus fulfilled by this bacillus. P. F.

Kolle, W., Schlossberger, H., u. Leupold, F. Untersuchungen an Tieren über die Verhinderung der akut tödlichen Wirkungen der Salvarsanpräparate. [**Animal experiments on the prevention of the acute fatal action of salvarsan compounds.**] *Med. Klin.*, 1920, **16**, 355.

Acute death or unpleasant symptoms such as collapse, dyspnoea, albuminuria, rashes, and other phenomena of an angio-neurotic character following the intravenous injection of salvarsan has suggested to many a similarity with the symptoms of anaphylaxis. The analogy is all the more striking as the untoward results usually appear after the second or third injections and but rarely after the first. The experiments made by Auer, Stühmer, Lesser, and Danysz have, however, not led to complete harmony in explaining the very serious results which may ensue during salvarsan treatment. Danysz (1916–17) has shown that rabbits inoculated with a fraction of the lethal dose of salvarsan will tolerate with impunity this same lethal dose administered twenty-hours later. In consequence, he recommended the preliminary use of a small dose before proceeding to the exhibition of ordinary therapeutic doses. The present authors confirm this in the case of mice injected with silver-salvarsan. One quarter of the lethal dose given twenty-four hours previously enables the animals to survive a lethal dose which will kill the controls. More extraordinary is the fact that there is a reciprocal protection of one salvarsan compound against others of a different chemical constitution. Thus a previous dose of old salvarsan will protect against a subsequent lethal dose of silver-salvarsan; colloidal salvarsan base will protect against silver-salvarsan, 'sulfoxylate' against sodium-salvarsan, and neosalvarsan against 'sulfoxylate'. Particularly marked is the protective action of colloidal salvarsan (obtained by dialysis) and silver-salvarsan, which has been presumed by Kolle to have a colloidal character. Indeed, the researches of Bauer (1919) have suggested that all the salvarsan type of bodies are semi-colloidal and behave as true colloids when injected into the body. Even collargol manifests a marked protective power against subsequent lethal doses of the homologous substance, but not much protective power against arsenical preparations of the salvarsan type. Sodium-salvarsan confers protection neither against itself nor against collargol, nor silver-salvarsan, colloidal salvarsan, or old salvarsan.

Sodium cacodylate—a crystalloid of the aliphatic series—produces no protection against the same substance, and but little against 'sulfoxylate'. Arsacetin produces a certain degree of resistance against fatal doses of 'sulfoxylate'. Colloidal indigo afforded no protection either against itself, collargol, or salvarsan. A table is presented to show that the greatest degree of protection (84 per cent. of the animals survived) was obtained against silver-salvarsan with previous injections of fractions of the lethal doses of silver-salvarsan or old salvarsan, colloidal salvarsan base, and to a less extent by collargol. The other compounds stood in the following order of protection: collargol (74 per cent.), old salvarsan (60 per cent.), neosalvarsan (59 per cent.), sodium-salvarsan (53 per cent.), and sulphoxylate (40 per cent.). The protection afforded by the first dose endures for two or three days and then gradually disappears.

All these results were obtained in mice, but nothing so marked appeared to obtain in the case of guinea-pigs. Indeed, the animals succumbed to the second dose in a shorter time than the controls. Occasionally, if the interval between the two doses was three days, a fatal result from the second dose was delayed. It was not found possible to render guinea-pigs passively anaphylactic by injecting them with the serum of a rabbit that had sustained, three weeks previously, an intravenous dose of 0·03 grm. silver-salvarsan per kilo. The authors take a stand against the anaphylactic theory of salvarsan injuries, and are also against the view of specific chemical combinations of the arsenical compounds with proteins in the body. They tend much more to the view that the mechanism is of a physico-chemical nature. Its practical importance is the possibility by small injections to increase the insusceptibility to the larger doses of a therapeutic order. W. B.

Ministerium des Inneren (Germany) Denkschrift des Ministeriums des Inneren über die Anwendung des Salvarsans und die dabei beobachteten Schädigungen der Gesundheit. [**Memorandum by the Ministry of the Interior on the application of salvarsan and the injuries to health observed therefrom.**] Berlin, Aug. 1918, 79 pp.

This is a memorandum issued by the German Ministry of the Interior, and deals with the accidents which are alleged to have occurred in connexion with the administration of salvarsan in the treatment of syphilis. The report is in three parts, with an appendix. The first part sets forth the events, political, social, and medical, which led to the inquiry, the second and third parts being the results of two inquiries, in 1914 and 1917 respectively, which were made to allay the anxiety of the public, whose interest in the subject had been aroused by a far-reaching press campaign for and against salvarsan. The early use of salvarsan, in 1909, the method of distribution of the drug by Ehrlich, and the results obtained from its use are well known. Within a year after it had been introduced it was recognized that unpleasant accidents may arise, and these were made the subject of widespread criticism, especially in certain sections of the lay press in Germany and elsewhere, and there arose two sets of people, salvarsan-upholders and salvarsan-opponents, who clamoured for its restriction or abolition as being devoid of value or actually dangerous. Further interest was created by the publication in 1913 of a small book, by Mentberger, of the Dermatological Klinik of the University of Strassburg. In this work it was alleged that up to date there had been 274 fatalities following injections of the new arsenical compounds. This was met with strong criticism by Benario, in Ehrlich's Institute, who showed that very few deaths were really attributable to the use of salvarsan. Further trouble was created by one Dreuw, a police surgeon, in Berlin—a violent opponent of the new treatment. He directed attention to what had already been called the 'salvarsan scandal' and considered that the drug should be prohibited, as it was dangerous and useless in the cure of syphilis, that the price was extortionate and the dose was grossly in excess of the maximal dose prescribed by the pharmacopeia for arsenic. Another press agitation broke out in which more than one doctor joined. Questions were asked in the Reichstag, the result being that in 1914 a memorandum of questions was issued to the directors of skin kliniks in the Prussian Universities, to large hospitals, and special kliniks for psychiatry and diseases of the nervous system. This memorandum was answered by 353 separate organizations on a material of 74,018 patients who had received 288,942 injections of salvarsan or neosalvarsan and Joha-Schindler. The manner of injection, the complications including deafness, blindness, neuro-recurrences, and deaths, are fully treated in the present report, from which it appears that the number of injuries was small considering the large numbers treated, and no fewer than 92 per cent. of those who made reports regarded the salvarsan as valuable or very favourable. The value of the report was, however, called in question by the salvarsan opponents and was alleged to be incomplete as it did not include the opinion of the general practitioners. It was further alleged that the questions were framed in such a way as to minimize salvarsan dangers and to magnify the dangers from mercury. Again the lay press took the matter up, and ultimately Dr. Dreuw presented a petition which came up for discussion at the Budget Commission of the German Empire on February 12, 1918, the result being that the Minister of the Interior ordered a new inquiry on a still wider basis. A series of 254 reports were obtained dealing with the treatment of 265,158 patients who had received altogether 1,268,946 injections of salvarsan or neosalvarsan. The details constitute the third part of the present memorandum issued by the German Government, and must be regarded as very favourable to salvarsan. Without entering into unnecessary details, the general results of the two series of cases will be easily understood by reference to the following table:

Number.	Inquiry of 1914.	Inquiry of 1918.
(1) of patients treated	74,018	265,158
(2) of injections made	288,942	1,268,946
(3) of neuro-recurrences	168 = 1 : 441 patients	100 = 1 : 12,700 patients
(4) of patients who died after receiving salvarsan	56 = 1 : 1,322 ,,	70 = 1 : 3,788 ,,
(5) of deaths caused by salvarsan	12 = 1 : 6,169 ,,	17 = 1 : 15,598 ,,

It has to be pointed out from this table that of the 12 deaths in the 1914 column there were 4 which are also included in the 1917 series. It was also ascertained that 3 deaths overlooked in the 1914 series must be added to that series, so that the total of the certain salvarsan deaths in the 1914 series was 15 instead of 12. Thirdly, between 1914 and 1917 there were 9 deaths in a series of patients numbering 191,140 (i. e. 265,158 of the 1917 series minus 74,018 cases of the 1914 series). Thus up to 1914 there were 15 deaths among 74,018 patients treated, a ratio of 1 : 4,935, whereas from 1914 to 1917 there were 9 deaths among 191,140 patients, a ratio of 1 death among 21,238 patients. The mortality due to pure salvarsan poisoning may thus be said to have diminished in 1917 to one quarter of what it was up to 1914. The general utility of the drug in syphilis and its relative absence of toxicity led the German Government to consider that there was no indication to interfere so as to prohibit its use as had been demanded in the petition of Dr. Dreuw. One would have thought that the scathing fire of criticism would now have been extinguished, but that this was not so is manifest from a new inquiry made by the General Medical Society of Cologne in 1918. The commission appointed by this body has also published a report which has already been reviewed in this Journal (1920, **2**, 529, 572).

W. B.

Herxheimer, G. Ueber akute gelbe Leberatrophie, Syphilis und Salvarsan. [**On acute yellow atrophy of the liver in relation to syphilis and salvarsan.**] *Berl. klin. Wchnschr.*, 1920, **57**, 369.

A short account of the pathological findings on six young adults who had been treated for early syphilis. All had received salvarsan and mercury treatment, except one who had been treated with mercury alone. Within four to six weeks all developed severe jaundice ending fatally in a few weeks. The autopsies showed the characteristic changes of acute yellow atrophy of the liver. In the recent medical literature of Europe there have been quite a number of cases of this kind, and although the cause is not ascertained it has generally been believed to be salvarsan or some such compound. The present author is not of this opinion, however, and inclines to the view that it is the syphilis itself that has brought about the change in the liver. He bases this opinion on the fact that severe jaundice terminating fatally was known and recognized long before the salvarsan days, although now apparently more frequent than formerly. Typical acute liver atrophy in syphilis untreated by salvarsan is identical with that in salvarsan-treated cases. He emphasizes the fact that the hepatic atrophy is met with almost exclusively in early stages of the disease, which is remarkable if it is to be attributed to salvarsan. Further, the characteristic encephalitis haemorrhagica so frequently found in cases of salvarsan intoxication does not occur in cases of acute or subacute atrophy of the liver. W. B.

Bock, G. Syphilitische Aortenerkrankungen und Wassermannsche Reaktion. [**Syphilis of the aorta and its relation to the Wassermann reaction.**] *Med. Klin.*, 1920, **16**, 447.

This is a record of 385 cases (3·97 per cent.) of syphilis of the aorta among 9,690 autopsies made in the Virchow Hospital, Berlin, between 1912 and 1917. The disease was found twice as often among males as females. Where the date of the infection could be ascertained it was found, among 50 cases, that 3 had developed the lesion within 10 years, the average period between the infection and death being 23·68 years. Among 339 cases 214 occurred between the 4th and 6th decade. The Wassermann reaction was found to be positive in only 66·47 per cent. of cases of undoubted luetic aortitis in this series. W. B.

Boas, H. Hvor lang Tid efter Infektionen med Syphilis bliver Wassermanns Reaktion positiv? [**How soon after infection with syphilis does Wassermann's reaction become positive?**] *Hosp. Tid.*, 1920, **63**, 369–73.

The material with which Boas has attempted to ascertain the length of the period between infection and the development of a positive Wassermann consists of 49 cases treated in 1910 at the Rudolph Bergh Hospital. Wassermann's reaction was carried out at the Serum Institute, and the antigen used was an alcoholic extract of the human heart. As it was impossible accurately to fix the date of infection on the basis of the patients' admissions, it was approximately fixed by counting 10 weeks back from the date of the first appearance of secondary symptoms. This method was the more reliable as treatment was not instituted till the appearance of secondary symptoms. Patients with chancres were tested by Wassermann's reaction every week until the appearance of a rash. It was found that in 35 cases the rash appeared in 1 to 7 days after Wassermann's reaction had become positive. In 2 cases the rash appeared 3 weeks, and in 4 cases 2 weeks, after the reaction became positive. In 5 cases the appearance of the rash and of a positive reaction were coincident, and only in 3 cases did the rash appear before the reaction became positive. Boas concludes from these figures that the interval between infection and the development of a positive reaction is usually 9 weeks, more rarely 7 or 8 weeks. C. L.

von Wedel, Hassow O. The complement-fixation test for tuberculosis. *J. Immunol.*, 1920, **5**, 159.

This is a very thorough investigation into the value of the complement-fixation test for tuberculosis, and in addition to a critical analysis of the results of others, from 1903 onwards, the author has himself made 6,128 complement-fixation tests on 1,207 sera taken from 1,000 patients. Of these sera 633 were from 484 patients in hospitals for tuberculosis, the remaining 574 sera being taken from 516 patients suffering from various other diseases. Comparative tests with 20 different tubercle antigens were made on 1,167 samples of serum obtained from 60 patients, and in addition tests were made with 60 sera by the Hecht–Gradwohl technique and by absorbing out their natural anti-sheep amboceptor. The following points were specially investigated: (1) the best general technique for the test and the optimum fixation time and temperature. (2) What antigen gives the highest possible percentage of specific positive reactions and none or only an occasional non-specific reaction? (3) Is there any advantage in using fresh active serum or in removing the natural amboceptor from inactivated serum? (4) Do the tubercle antigens, found to be most effective, give any non-specific cross-fixation with syphilitic sera? (5) Is there any relationship between the fixation test and the age, temperature, pulse, or respiration of the patient? (6) What is the best method of classifying tuberculous patients from the combined point of view of the serologist and the clinician? (7) What type of tuberculosis gives the highest percentage of positive reactions? (8) What value has the reaction to the clinician as an aid to diagnosis and prognosis?

The general technique employed was that of the original Wassermann test for syphilis, in one-tenth volumes, however. The complement was obtained from single guinea-pigs or from the pooled serum of groups of 6 to 10 guinea-pigs, the most constant results being with 2 haemolytic units of selected complement combined with red cells which had been sensitized with 3 units of amboceptor. As a standard antigen Wilson's method of preparation (*J. Immunol.*, 1918, **3**, 345) was used throughout the series. This consists in suspending in 0·9 per cent. saline, dried tubercle bacilli from which all constituents soluble in alcohol and ether have been removed. The anticomplementary action of the antigen was determined in separate experiments. The sheep's corpuscles were washed five times with sterile saline, and were then sensitized with 3 units of amboceptor. Various experiments were made to determine the optimum time and temperature for fixation, and this was found to be 37° C. for 1 hour. Extensive tables are presented to illustrate the effect of heat on the anti-sheep haemolysins in human sera, and the conclusion is reached that natural anti-sheep haemolysin is markedly thermolabile when heated to 56° C. If the serum is kept sterile the natural anti-sheep lysin does not deteriorate very rapidly. Hitherto investigators have used four different types of tubercle antigens which may be classified as follows: (1) Antigens composed of the whole bacillus. (2) Various tuberculins. (3) Antigens derived from the bacilli by means of chemical digestion ('partial' antigens). (4) Antigens derived from normal or tuberculous tissues. The consensus of opinion is in favour of the first group, a choice lying between the living bacilli in suspension or killed by chemicals or heat. The author believes in the latter, and his experiments indicate that even a temperature of 100° C. for 3 hours does not seem to impair the antigenic properties of a bacillary suspension. He also considers that an increase in positive results can probably be obtained by absorbing the natural anti-sheep amboceptor before making the test, or by using the fresh active serum advocated by Hecht and Gradwohl. It is pointed out, however, that such modifications give a moderate percentage of non-specific reactions, and they should only be used as control tests along with the standard technique. On the sera of 900 patients (500 tuberculous and 400 non-tuberculous) comparisons were made to determine whether the results on the sera one day old agree with those when the same sera have been kept one week in the ice-chest. The latter gave a higher percentage of positive results, which, however, were non-specific and apparently due to anticomplementary changes and non-specific variations in the reagents employed in making the tests. In a large number of sera the author tested the Wassermann as well as the tubercle-fixation reaction, and found no evidence of cross-fixation with the antigens employed by him—a result at variance with the recent expressions of Corper, who concluded that in the presence of a positive Wassermann reaction the existence of a positive fixation test for tubercle has no practical significance. The results of von Pirquet reactions were apparently not parallel with those of the fixation reactions.

For many years much attention has been given to the question of the classification of different forms and stages of pulmonary tuberculosis, but with indifferent success. One of the most recent attempts at classification, viz. that of Rathbun, which has been accepted by the American Sanatorium Association, classifies cases into 'incipient' A, B, and C; 'moderately advanced' A, B, and C; and 'far advanced' A, B, and C. The present author points out that this classification disregards the activity of the diseases manifested by one and the same patient at any given time. As the basis of the fixation test is presumably the degree of antibody production in the patient's serum, and as this production is based, primarily, on the activity of the disease irrespective of its clinical stage, no parallelism can be expected between this classification, and the test under investigation. The author had (1918) suggested another classification, but found it was not interchangeable with that most commonly employed by clinicians. In general, however, it appeared that the largest percentage of negative and weak positive results were found in cases having few or no constitutional symptoms, while the strength and incidence of positive reactions increased progressively with increased constitutional symptoms until the patient is reaching the advanced stage when the reverse is true. As the patient loses his powers of resistance the complement fixation reactions tend to swing towards the negative side. The age of the patient was found to have no apparent influence on the fixation test. Extensive tables are presented of six series of complement-fixation tests made at different hospitals, and in conclusion the author sums up his researches by the assertion that the fixation test is not a 'hundred per cent.' one for the diagnosis of tuberculosis. A considerable percentage of sera from incipient and far advanced cases of consumption contain insufficient antibodies to fix complement, no matter what system or what antigen is employed for the test. This is in agreement with most of the findings of other investigators. About 70 per cent. positive results appears to be the average findings when all types of unselected active cases of tuberculosis are taken into account. The reactions are weakest when the patient exhibits few, if any, symptoms of the disease, while they are most definite and strongest in the incipient and moderately advanced cases exhibiting marked symptoms. The results are therefore confirmatory rather than actually diagnostic in the largest percentage of cases. In the author's opinion a positive reaction obtained twice on the same patient seems to prove fairly conclusively that the patient has an active tuberculous process. The weakening of the reaction from a strong positive to a weak positive or negative reaction is apparently a good prognostic sign in incipient and moderately advanced cases exhibiting clinical improvement, while at the same time this change with a far advanced case in a poor clinical condition is a very bad prognostic sign. W. B.

Kolmer, J. A., and **Matsumoto. Natural antihuman hemolysins and hemagglutinins in horse sera in relation to serum therapy.** *J. Immunol.*, 1920, **5**, 75.

The intravenous injection of human beings with large amounts of serum from immunized horses—as in the treatment of pneumonia—is sometimes followed by symptoms which cannot be referred to anaphylaxis. The present investigation was made by testing for haemagglutinins and haemolysins to find out whether intravascular agglutination and haemolysis might, if they existed, be responsible for the symptoms. Normal and immune horse sera were tested *in vitro* on the red blood cells of different people, and the effects of agglutination and haemolysis *in vivo* were determined in rabbits as it was found that horse sera contained agglutinins and lysins for the blood corpuscles of this animal. It was found that nearly all horse sera contain agglutinins for human erythrocytes, being highest in fresh sera and disappearing, largely, in sera preserved by such an antiseptic as tricresol. Fresh horse sera may also contain antihuman haemolysins, but the latter are only occasionally found in old or preserved sera. The intravenous injection, into rabbits, of large amounts of horse sera containing agglutinins and lysins for the erythrocytes of rabbits produces no ill effects or symptoms that could be referred to intravascular agglutination or haemolysis. It is unlikely that the deleterious effects, occasionally observed when persons are injected with horse serum, are due to intravascular agglutination or haemolysis. W. B.

Kolmer, J. A., and **Trist, Mary E. An attempt to produce specific immune agglutinins and hemolysins for the four groups of human erythrocytes.** *J. Immunol.*, 1920, **5**, 89.

This paper contains the results of experiments made to determine whether it is possible to evoke the production of agglutinins and haemolysins specific for each of the four groups of human erythrocytes by immunizing rabbits with the red corpuscles of Groups I, II, III, and IV. The results were disappointing in that the inoculation of rabbits with human red corpuscles of one or other of these groups did not lead to the production of specific agglutinating or haemolytic sera, although the titre for the homologous group was frequently higher than for the heterologous group. Absorption of the immune sera to remove the group agglutinins generally resulted in the removal of all agglutinins and lysins. For the grouping of human erythrocytes it does not appear to be possible to prepare specific immune sera.

Human sera containing isoagglutinins and isolysins must be used, and these are best preserved in the fluid state at or near the freezing-point.

W. B.

Allen, F. M. Experimental studies on diabetes. Series I. Production and control of diabetes in the dog. *J. Exper. M.*, 1920, **31**, 363, 381, 555, 575, 587.

Jensen, V. W., and **Carlson, A. J. The apparent influence of a diet of carbohydrates on the pancreas remnant of partially pancreatectomized dogs.** *Am. J. Physiol.*, 1920, **51**, 423.

The first of these is a series of five elaborate papers from the Rockefeller Institute, each with a special subtitle by the well-known authority on the modern methods of the treatment of diabetes. 'The basis of these studies', he says, 'has been a form of diabetes produced by removal of the greater part of the pancreas of animals, leaving a remnant about the duct secreting normally into the duodenum, thus avoiding the rapidly fatal cachexia of total pancreatectomy and also the pancreatic sclerosis and deficient digestion of Sandmeyer diabetes, and affording a very close and satisfactory reproduction of the clinical disorder.' A summary is first given of the anatomical facts, in dogs, with regard to the mass of the pancreas, the body mass, and the size of the remnant with which diabetes occurs. A detailed record was kept of the sex, apparent age, breed, colour, and character of coat of all the animals. Analysis indicates that sex is immaterial, and that in adult animals age variations are without perceptible influence in regard to the weight of the pancreas. No breeds were found with characteristically large or small pancreas. Dogs offer unique advantages for tracing a range of relations between body weight and pancreas weight. No other mammal exhibits such a gamut of sizes for normal adults of the same species. Small dogs generally possess more pancreatic tissue in proportion to their body mass than large dogs. Observations were also directed to determine whether a uniform mathematical law can be established for the occurrence of diabetes whenever a fixed proportion of the pancreas is removed, or whether general or individual exceptions exist. The author's present figures confirm previous findings (see Allen, F. M., *Studies concerning Glycosuria and Diabetes*, 1913, Cambridge), that, with few exceptions, mild diabetes occurs when the remnant is $\frac{1}{8}$ to $\frac{1}{9}$ of the pancreas, and severe diabetes when the remnant is $\frac{1}{10}$ of the pancreas. A partially depancreatized animal, which has merely a lowered tolerance and cannot be made diabetic by any quantity or duration of feeding, may be so close to the verge that diabetes results from the removal of only a fraction of a gramme of additional pancreatic tissue. Likewise, definite variations in the severity of diabetes may be produced, e.g. by overfeeding.

Diabetes was not found to be a determining factor in hypertrophy of the pancreas remnant, which was present or absent in diabetic and non-diabetic animals indiscriminately. The stimulus did not apparently originate from lack of either the internal or external function of the pancreas. A still more important question is to what extent the hypertrophy was able to preprevent or cure diabetes. In some instances the new-formed tissue appeared functionally equivalent to the old, for, not only was diabetes checked, but to reproduce it a further resection of tissue was necessary to reduce the remnant to the size requisite in the original operations. On the other hand, diabetes sometimes stopped when there was little or no hypertrophy of the remnant. Hypertrophy was also frequent, with a continuance of the diabetes.

A closer study of these results, which appear at first to be contradictory, brings out the following explanatory facts. The traumatic inflammation following operation is generally a factor in producing diabetes in cases with fairly large remnants. Inflammation may injure chiefly the islets, to such an extent that the animal remains diabetic after the inflammation has subsided, notwithstanding hypertrophy of the remnant. If a functional injury may be assumed, as seems to be true in human diabetes, an explanation is afforded of the existence of diabetes even when the hypertrophic remnant contains numerous islands, but this point is still doubtful. Overfeeding furnishes the most frequent explanation, and may be put to valuable use. For example, severe acidosis is obtainable only when the dogs can digest large quantities of fat, and dogs with small pancreas remnants can seldom do this. But by cautious overfeeding with carbohydrate after operation, mild diabetes may be kept up, while in a certain proportion of animals marked hypertrophy of the remnant is taking place. Islands are thus injured or destroyed, while the great increase of acinar tissue enables a satisfactory digestion of fat. Experiments show there is no warrant for attempting to stimulate regeneration of the human pancreas by mere trauma. The records of puppies in a subsequent paper indicate no remarkable regenerative activity, just as the damaged pancreas of diabetic children fails to recover to any greater extent than that of adults. The suggestion of some writers that animals may develop 'immunity' to the lack of pancreatic tissue, particularly by the vicarious action of other glands, is not borne out by the author's experiments of repeated operations—two to five in number, with the intervals between them ranging from 2 weeks to 32 months.

At the commencement of the second paper the author remarks: 'The belief underlying the dietetic treatment of diabetes has been that the disorder consists in the weakness of a bodily function which is broken down by overstrain and spared or strengthened by rest. A co-existent and equally firmly noted belief has been that some or perhaps most human cases are inherently progressive, on account of continuing toxic, infectious, or undetermined factors, so that they become worse and lead to death after a longer or shorter time in spite of dietary restrictions.' The author does not consider that the fundamental question of the possibilities and limitations of injuring assimilation and shortening life by overfeeding, and the improving of tolerance and the lengthening of life by restricted diet to be fully settled by previous experiments. He has, therefore, carried out a fresh set of experiments to determine the effects of carbohydrate diets.

The injurious effects of excessive carbohydrate diet are demonstrable in partially depancreatized dogs in the same manner as in human patients. With severe diabetes there is rapid progress of emaciation, weakness, and early death.

With milder diabetes, there is often a transitional state following operation, when the fate depends on the diet. If the tolerance is spared for a time, recovery sometimes occurs to such extent that diabetes cannot be produced by any kind or quantity of feeding, but only by removal of a small additional fragment of pancreatic tissue.

In the early stage, glucose is more powerful than starch in producing diabetes, and animals progressing towards complete recovery on starch diet can be sent into hopeless diabetes by admixture of glucose. The difference seems to be merely of the rate of absorption, and indicates that a rapid flood of carbohydrate is more injurious to the pancreatic function than a slow absorption. Whenever permanent diabetes is present, so that complete recovery is impossible, starch brings on glycosuria more slowly than sugar, but just as surely. The clinical lesson from such experiments is that even if a patient becomes free from glycosuria on withdrawal of sugar only, nevertheless, other foods should also be limited. No significant differences were observed between the assimilation of different starches, or any extreme lowering of the carbohydrate tolerance by proteins, such as alleged by certain writers in connexion with the 'oatmeal cure'. Repair of traumatic inflammation and hypertrophy of the pancreas remnant seem to be the basis of the early tendency to recovery, and also hydropic degeneration of the islets of Langerhans to accompany the lowering of tolerance by excessive diet. These are believed to have their parallels in human cases, and are to be described more fully later on.

Then follows a comparison of the effect of protein and carbohydrate in producing glycosuria. If the dogs are mildly diabetic it is found that the starch of 50–100 grm. of bread or cereal is more active in producing glycosuria than the larger quantity of potential carbohydrate represented in a kilo of ox lung. There is no doubt the starch would be much better assimilated if distributed in small doses over a longer time. A set of facts is brought forward to show that the difference cannot only be one of rapidity of absorption and metabolism. The maximal dextrose-nitrogen ratios in the severest diabetes are a familiar proof that the carbohydrate of protein is excreted quantitatively and is as incapable of assimilation as preformed carbohydrate. These facts conform to clinical observations, and justify the earlier treatment of diabetes since the restriction of preformed carbohydrate is the basis of dietotherapy, and protein restriction comes secondary both in time and importance. No specific differences were observed between the glycosuric effects of different kinds of protein. The following are some of the author's conclusions:

1. Practically every detail of clinical diabetes can be reproduced in partially depancreatized animals. The resemblance is made still more exact by the susceptibility of such dogs to acidosis and coma and to the similarity of the anatomical changes in the islands of Langerhans.

2. These animals at first show considerable tendency to regain assimilation, comparable to that in the early stages of most human cases of diabetes; and in some instances they recover so as to be able to endure any degree or duration of carbohydrate feeding, and can be made diabetic only by removal of additional pancreatic tissue. Similar recovery in some human cases, especially after acute pancreatitis, is a probability. This recuperative tendency can be negatived by overfeeding, even without glycosuria. With duration of the diabetes the power of recuperation diminishes and practically disappears in dogs as in human patients.

3. In the absence of progressive pancreatitis or other extraneous causes, these dogs show no inherent downward tendency in their assimilation.

4. Every detail of the downward progress of human patients on various diets is reproduced in such animals. They lose assimilation and die most rapidly on diets rich in carbohydrate, and less rapidly on excess of other

foods. The differences between sugar and starch, and between starch and protein, seem to be only those of degree and time rather than anything absolute. Granting the absence of spontaneous downward tendencies, all the different kinds and degrees of downward progress in the animals studied are purely the results of overstrain of the internal pancreatic function by excess of food.

5. The benefit of the classical treatment by exclusion of preformed carbohydrate and limitation of protein is confirmed, in the prolongation of life and well-being, to some extent in nearly all cases and perhaps indefinitely in some of the mildest cases. In the great majority of cases such a therapeutic result is not permanent, and downward progress is finally observed if the observations are continued long enough. In most of these cases life, strength, and assimilation can be preserved for a much longer time by a degree of under-nutrition suited to the severity of the diabetes, and accomplished by limitation of fat in the diet. The permanence of such control is supported by the unimpaired or rising assimilation in experiments of 1 to 1¾ years' duration, but still longer observations would be desirable. Diabetes of great severity is controllable only by correspondingly radical under-nutrition. In still more severe cases, glycosuria can be abolished only by a degree of under-nutrition which entails final death from inanition. In the most severe cases, glycosuria cannot be stopped, evidently because the assimilative power is too low to dispose of even the minimum supply of food materials; namely, that derived from the body stores in fasting.

6. The basis of the belief in the inherently progressive tendency of severe cases of clinical diabetes is shaken by the exact reproduction of such case-histories by diet in animals which are free from spontaneous downward tendencies; but there is still lack of a sufficient number of patients treated on the principle of relief of the total metabolic burden to demonstrate the absence of such inherent progressiveness in human diabetes. The principle mentioned has given encouraging results in proportion as it has received actual application in practice. The clinical problem requires the same prolonged careful control of all discoverable symptoms as in animals, and cases too severe for such control, or complicated with infections, violations of diet, &c., are on the same plane as animals in which a similar condition has been produced. Some proportion of cases, especially in young persons, will be found suitable for accurate determination of the question of whether all or most cases of severe diabetes are inevitably progressive and hopeless. On the theoretical side this question involves both the general prognosis and the nature of the process underlying diabetes. On the practical side it is already established that the diet is at least the chief cause of downward progress, and it is important to eliminate this cause by avoiding the dietary injuries illustrated in the animal experiments.

In the second research by Jensen and Carlson, working in the Hull Laboratory, University of Chicago, ground is covered very similar to that in the above reviewed papers of Allen. The object of the experiments was to determine more definitely whether a carbohydrate diet prevents pancreatic hypertrophy, or induces pancreatic degeneration after partial pancreatectomy. Comment is made on the fact that previous investigators have reported no 'control' dogs. Care was taken in the preparation of the dogs that the pancreas remnant was connected with the duodenum through the main duct, and that this duct was patent. Also, that each animal after the partial pancreatectomy showed no glycosuria on a liberal protein diet, but showed persistent glycosuria on a carbohydrate diet. Three different types of diet were used—one containing 60 per cent. of carbohydrate, another a low percentage of carbohydrate, and the third was essentially protein. Water and meat-free bones were supplied *ad libitum.* Twenty-four hour samples of urine were collected. In general the results support the view that a liberal carbohydrate diet tends to change diabetes *levis* into diabetes *gravis* after partial pancreatectomy in dogs, but the experiments are not more conclusive than the earlier ones of Thiroloix and Allen. The authors consider that the question can only be settled by the statistical method, using many animals for the work, for one cannot predict the metabolic course of any one animal deprived of approximately seven-eighths of its pancreas. When a considerably smaller pancreas remnant is left the dog passes into fatal diabetes irrespective of the diet; and if the remnant is somewhat larger no amount of forced carbohydrate feeding induces diabetes *gravis.* Moreover, the functional efficiency of the pancreas appears to vary in different dogs, so that the estimation by weight of the optimum pancreas remnant for the solution of this question involves a large and variable error. The authors consider that the analogy from an impaired digestion is not to the point. It is true that ingesting certain foods, or any food in certain amounts, may aggravate the untoward condition of an alimentary tract whose digestive juices and motor power are much below normal, but this is not due to any ‘overstrain’ of the digestive glands, or of the gastro-intestinal motor mechanisms. It is due to stasis, bacterial fermentation, and putrefaction, and to abnormal reflexes evoked from an hyperirritable gut.

When the functional capacity of the pancreas remnant is too small to prevent diabetes, the remnant undergoes practically no hypertrophy. On this point the authors' results are in agreement with those of previous workers. This failure to hypertrophy may be due to the unfavourable influence on growth in general of the diabetic condition, rather than to specific ‘overstrain’ of the pancreas remnant. The favourable effects, at least in many cases, of partial starvation in the management of diabetic patients cannot at present be ascribed, in whole or in part, to relieving an impaired (endocrine) pancreas from the overstrain of ordinary diets, in view of the indications from human and comparative physiology that starvation, within limits, tends to rejuvenate tissues in general. W. A. M. S.

LAUNOY, L. Étude sur le pouvoir antitryptique du sérum sanguin. [**Study on the antitryptic power of blood-serum.**] *Ann. de l'Inst. Pasteur,* 1919, **33,** 1.

LAUNOY, L. De l'action antagoniste du sérum sanguin de quelques mammifères sur les protéases microbiennes. [**On the antagonistic action of the serum of certain mammals, on microbic proteases.**] *Ibid.,* 1919, **33,** 657.

LAUNOY, L. Les sérums antiprotéasiques, leur spécificité, la réaction de l'antiprotéase. [**Antiprotease sera, their specificity and the antiprotease reaction.**] *Ibid.,* 1920, **34,** 249.

The author considers that the readiest methods in use for the determination of the antitryptic action of blood-serum are those of Marcus and Gross-Fuld. Various criticisms are made on the technique employed, with the result that the methods are not considered sufficiently rigorous. The object of this paper is to show an exact method of numerically representing antitryptic power. The sera of man, horse, guinea-pig, sheep, rabbit, fish, eel, birds were used. The method of the rennet action of trypsin used by Achalme and Stévenen is considered to be free from the objections he has raised, and so he seeks to improve on the above methods.

Gelatin is chosen as the substrate, contrary to the fact that most workers have rejected it. The author considers that its purification by dialysis removes the most important objection to its use. Unit test solution (gelatin) and unit tryptic solutions are devised. Free acidity, and also that produced by the action of formol, are estimated by N/10 NaOH. The temperature of digestion is 41° C., and time is reckoned in hours. A great variety of conditions is investigated, and the results plotted graphically. Each graph shows the free acidity, the acidity produced by formol, and the total acquired acidity. The graphs at first diverge, but after a period of about 30 hours' digestion they tend to become parallel.

The results obtained are used to compare the antitryptic powers of two sera. The experiments incidentally show the strict relation between the sera of the above-mentioned animals, and their antitryptic power, as is also the fact that lipoids seem to have no influence on this antitryptic power.

In the second paper the author applies the above method to the comparative study of the action of blood-serum on the one hand against the trypsin of animals, and on the other hand against bacterial proteases. It is found that there is a considerable difference in the intensity of the proteolysis of gelatin in a trypsin blood-serum medium as compared with that in a bacterial protease blood-serum medium. In the first case, for a sufficient amount of serum the proteolysis is nil or practically so, while in the second case, even in the presence of excess of serum, proteolysis always occurs. The blood sera of man, horse, rabbit, and guinea-pig do not possess, as opposed to bacterial proteases, the inhibitory properties which the latter show towards the pancreatic trypsin of mammals.

The action of blood-serum on the proteases of *B. pyocyaneus*, *B. prodigiosus*, *B. proteus*, *Vibrio cholerae* (Zarizin) is characterized by a diminution of their enzymatic power and by a slowing of their action—the order of slowing of the three sera particularly studied being that of the horse, man, and lastly, rabbit.

Above a certain volume of serum (0·1–0·2 c.c.) the inhibitory action on the proteases vanishes, giving place to a favourable action.

In the third paper the author considers the possibility of obtaining artificially, real bacterial antiproteases, and the question of their specificity. These points have been considered by others, notably Von Dungern, Moreschi, Hata, and Kurt Meyer, but as their results are of a qualitative nature the author seeks to repeat the experiments quantitatively. He uses the method already described above for the antagonistic action of blood-serum on pancreatic trypsin and on bacterial proteases. His conclusions are:

1. A subcutaneous injection, into a guinea-pig, of a bacterial proteolytic filtrate results in the formation of antibodies, which are strictly specific.

2. The specificity of the antiprotease obtained by the injection of the filtrate from a culture of *B. pyocyaneus* extends to all varieties of this bacillus.

3. The reaction of pyocyanic antiprotease permits a characterization of the different members of this group, degraded from a pigmentary point of view, but still possessing the property of secreting the protease. It also

allows of a separation from other fluorescent bacteria which are non-pyocyanic.

4. The action shown by an antiprotease serum on a tryptic unit is of the same order as that of normal sera, sometimes perhaps slightly augmented.

5. The antiprotease action of agglutinins divides them off from others. It is also shown that agglutinins can form without the simultaneous appearance of antiprotease. To this point the author intends to return later.

W. A. M. S.

BIOCHEMISTRY

Gamble, J. L., and Blackfan, K. D. Evidence indicating a synthesis of cholesterol by infants. *J. Biol. Chem.*, 1920, **42**, 401.

The authors have propounded the question as to whether the organism can synthesize cholesterol or not. Since many sterols are present in the tissues of plants, it is not inconceivable that cholesterol may be derived from the food. Indirect evidence bearing upon this is the re-utilization of cholesterol after its excretion in the bile, showing a need for the conservation of this substance within the body. The authors have used infants for their studies. They have compared the intake and excretion of cholesterol, after obtaining a knowledge of the amount of cholesterol fed in the diet. The argument is that if infants gaining in weight upon their diet show a positive balance in favour of cholesterol intake, it is probable that the tissue cholesterol is being derived from the food cholesterol. On the other hand, if there is a regular negative balance, it means that the organism must be synthesizing cholesterol. They found that there was excreted in the faeces during the experimental period from 1·4 to 3·4 times the amount of cholesterol present in the food, and interpret this to mean that cholesterol is synthesized in the organism. R. A. P.

Ziegler, M. R., and Pearce, N. O. A metabolic study of amyotonia congenita. *J. Biol. Chem.*, 1920, **42**, 581.

The special features of distinction are a lowered creatinin excretion, together with the excretion of creatin upon a low protein diet; a normal uric acid excretion; an increased rest nitrogen, with an increased neutral sulphur excretion; a normal phosphorus excretion; and a lowered chloride excretion. R. A. P.

Hart, E. B., Steenbock, H., and Ellis, N. R. Influence of diet on the antiscorbutic potency of milk. *J. Biol. Chem.*, 1920, **42**, 383.

The antiscorbutic vitamine is supposed to come from the plant or food from which it is excreted into the milk by the mammary gland. If this is so the milk produced upon a poor antiscorbutic diet should be less potent as a source of antiscorbutic vitamine than the milk produced upon a diet rich in this factor. Experiments by these authors show that, in the case of cows' milk, summer pasture milk is richer in the antiscorbutic element than dry feed milk or winter produced milk involving the use of corn, silage, or sugar mangels as part of the ration. R. A. P.

Osborne, T. B., and Mendel, L. B. The occurrence of water-soluble vitamine in some common fruits. *J. Biol. Chem.*, 1920, **42**, 465.

The fresh juices of the orange, lemon, and grape-fruit all contain a good supply of water-soluble B. vitamine. Apples and pears do not contain nearly as much. Prunes are slightly richer than apples and pears. Hence all fruits cannot be considered as equally effective in supplying this vitamine. R. A. P.

Allen, F. M., and Wishart, M. B. Experiments on carbohydrate metabolism and diabetes. I. Intravenous glucose tolerance of dogs. II. The renal threshold for sugar and some factors modifying it. *J. Biol. Chem.*, 1920, **42**, 415; **43**, 129.

The authors have been engaged in an interrupted research upon the relation between hyperglycaemia and glycosuria in pancreatic diabetes. They have used the dog for their experiments. The experimental method has been the following. Instead of feeding their animals with sugar (to determine this sugar tolerance) they have injected a known amount of glucose into the circulation. For this purpose they have used a convenient vein and accustomed their dogs to the operations involved (which do not give pain). The injection method has the advantage of giving an exact measure of the amount of glucose injected instead of a doubtful amount absorbed from the intestine. The dogs show a good resemblance to the findings of clinical cases. The main conclusions reached at present are as follows: animals made diabetic by the removal of the pancreas under ether anaesthesia have a diminished renal permeability for glucose. This means that it is necessary to raise the blood-sugar to a higher percentage than the normal before sugar is excreted in the kidney. This is similar to the case of the great majority of human diabetics.

Why does this happen? The usual teleological explanation is that it is an attempt upon the part of the body to conserve supplies of sugar. The authors have found, however, that there may be a raised sugar threshold from several extraneous causes. For instance, an injection of epinephrin resulted in a rise of the sugar threshold of the kidney in the normal animal. High fat diets may also raise the sugar threshold in diabetic dogs even in the absence of any acidosis. The raising of the sugar threshold, if accompanied by a decreased permeability of the kidneys to other metabolic products, is not likely to be of much help to the body. They do not think it likely, in view of the number of extraneous causes that may raise the threshold, that there is a protective mechanism involved.

These experiments upon animals have the great advantage that they give results independent of kidney and other disorders, which so often obscure the clear clinical picture of diabetes. R. A. P.

Brown, W. H., and Pearce, L. On the production of generalized syphilis in the rabbit by local inoculation. *Proc. Soc. Exper. Biol. & Med.* 1920, **17**, 167.

Generalized syphilis in rabbits is not easily produced. There occurs instead an intense local reaction. By suppression of the primary lesion by an arsenic compound, which had a greater effect on the resolution of the lesion than on the spirochaete, and by early removal of the medium of inoculation, and then by preventing a primary reaction, it was possible to produce a well-defined general syphilis. An inhibitory influence is exerted on the general condition by the reaction taking place at the seat of inoculation, which is proportional to its severity. Suppression of this local reaction gives rise to a general syphilis. C. G. L. W.

Cohn, A. E., and Levy, R. E. The effect of therapeutic doses of digitalis on the contraction of heart muscle. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 160.

Direct experiments with the myocardiograph, combined with electrocardiograms and blood-pressure records, showed that doses of digitalis and strophanthin, 30 per cent. of the lethal dose, increased the contractile power of the cardiac muscle, and by so doing increased the volume output. There is, therefore, a sound basis for the therapeutic action of these drugs.

C. G. L. W.

Rous, P., and McMaster, P. D. A. Vicious activity of the gall-bladder during biliary stasis. B. The determining factor in the causation of white stasis bile. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 159.

Ligation experiments in animals show that under stasis conditions the gall-bladder and bile-ducts act very differently. The gall-bladder effects a concentration of the bile and adds mucus to it. When an obstruction is produced below the entrance of the cystic duct all the extra lobular biliary channels become filled with a thick greenish-black fluid. In an obstructed duct system blocked off from the gall-bladder a watery fluid is produced devoid of pigment and bile salt, even when the animal is heavily jaundiced. This is the 'white bile' of the surgeons. The facts point to cholecystectomy as a wise measure in gall-stone cases, and notably when the gall-bladder is but little damaged. The frequent rapid increase in size of gall-stones partially obstructing the common duct is attributable to the concentration of stasis bile by the gall-bladder. C. G. L. W.

Papanicolaou, G. N., and Stockard, C. R. Effect of under-feeding on ovulation and the oestrous rhythm in guinea-pigs. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 143.

The follicle within the ovary is sensitive to changes in environmental conditions, one of which is the quality of the food. In guinea-pigs a late and long under-feeding may delay ovulation for eleven days. The variation in the oestrous cycle in rats which have been observed may be due to variation in the quantity of food consumed. C. G. L. W.

Levine, M. The behaviour of crown-gall on the rubber tree (*Ficus elastica*). *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 157.

The work is an attempt to show the processes analogous to human cancer which take place in plants. *Ficus elastica* is a very suitable plant for use in these studies. When *Bacterium tumefaciens* is inoculated into the apical internode of the branches, or into the leaves or main stem, a new growth is stimulated which may be either benign or malignant. Portions of the stem above and below the gall so produced may die. It is possible that the products of the disintegrating crown-gall or of the organism producing it are carried into the circulation and produce necrosis above and below. The death of the plant is at least suggestive of the death caused by the invading and disintegrating malignant growths in animal cancer. C. G. L. W.

Longcope, W. T., and **Mackenzie, G. M. The relation between the disappearance of foreign proteins from the circulation and the formation of antibodies.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 133.

Cases were studied that had received 100–500 c.c. of horse serum containing antipneumococcic bodies. The duration of the horse serum in the organism and the appearance and curves of precipitins were followed by specific reactions.

The cases fall into practically two groups. In the one group the horse serum persisted for 18–39 days, and the precipitins appeared between the sixth and fifteenth days. All these cases suffered from serum sickness. In the second group the horse-serum reaction persisted for 49–67 days. The precipitin reaction was either negative or very slight. None of these cases had anything but a very mild serum disease lasting from 1–5 days.

In one exceptional case the serum persisted for over 75 days and showed precipitins. This case had a severe attack of serum sickness lasting 12 days.

It is suggested that insusceptible persons have some protective mechanism which prevents or delays the union of the antigen with the cells of the body. C. G. L. W.

Faber, H. K. Sodium citrate and scurvy. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 140.

Sodium citrate, when added even in small amount (0·25 per cent.) to raw cows' milk, destroys the antiscorbutic qualities of the latter.

C. G. L. W.

Burge, W. E. Comparison of the catalase content of the tissues of the mother and of the offspring. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 129.

It is now considered that metabolism is low during the first month of life, high during childhood, and low after the onset of old age. The author has confirmed earlier work of Battelli and Stern, and has shown that the catalytic activity of the liver of puppies, ten weeks old, was about 30 per cent. greater than that of the mother. The low metabolism in the new born is attributed to the low catalase content of the tissues.

C. G. L. W.

Macht, D. I., and **Satani, Y. A study of local anaesthetics in respect to their antiseptic properties.** *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 128.

Cocain and novocain possess no antiseptic properties.

Among those which display distinct antiseptic characters are benzyl, alcohol, beta-eucain, and holocain. C. G. L. W.

Eddy, W. H., and Stevenson, H. C. Further studies in the measurement of vitamine content. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 122.

The authors have developed the method of measuring vitamine content by determining the effect of these substances on the growth of yeast. The improvements are concerned with the employment of the Wright capillary pipette as used in the opsonin technique. The method appears to be a convenient one. C. G. L. W.

Rose, M. S., and MacLeod, G. Some human digestion experiments on raw white of egg. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 119.

The raw white was as well digested as the cooked, if beaten light. A difference of 11·0 per cent. was observed in the digestion coefficient when the egg-white was swallowed without subdivision. C. G. L. W.

Thro, W. C., and Ehn, M. Calcium in the blood in disease of the skin. *Proc. Soc. Exper. Biol. & Med.*, 1920, **17**, 116.

Before proceeding with the treatment of furunculosis by salts of calcium it was thought advisable to estimate the amount of calcium in the blood in cases of boils. The amount of calcium was found to be low, while in cases of acne the calcium is increased. In boils the amount varied from 5·0–11·8 mg. of Ca per 100 c.c. of plasma, while in acne the concentration of calcium varied between 10·7 and 25·7 mg. per 100 c.c.

C. G. L. W.

Hirsch, P., u. Mayer-Pullman, R. Untersuchungen mit Hilfe der interferometrischen Methode zum Studium der Abwehrfermente bei Rindertuberkulose. [**The detection of protective ferments in bovine tuberculosis with the interferometer.**] *Fermentforschung*, 1920, **4**, 64.

It is assumed that in certain infections protective ferments are formed which are capable of digesting the infective agent. This is an elaboration of the Abderhalden theory, in which it has been claimed that similar ferments are formed in pregnancy, cancer, and many other conditions.

The authors have attempted to determine whether the serum of animals infected with bovine tubercle bacilli is capable of digesting tubercle bacilli and organs which were frankly tuberculous. The determination of a digestive process was made with the interferometer, which allows a very delicate detection of protein digestive products. Controls were made of the animals by macroscopic and microscopic examination after slaughter. Animals, usually young ones, free from infection, were used as controls. A certain number of sick animals which were non-tuberculous were also used. Non-tuberculous organs were also used as control substrates.

In only one case out of forty examined was a non-tuberculous serum found to digest tubercle bacilli, which is explained by a previous healed lesion. Very similar results were obtained for tuberculous organs. If the results can be confirmed in human tuberculosis, another method will be available for the detection of the disease. The amount of serum necessary for a test is only 0·5 c.c. C. G. L. W.

Lamson, P. D., and Nagayama, T. Blood-volume and blood-volume methods. *J. Pharmacol. & Exper. Therap.*, 1920, **15**, 331.

Histamin is not the active principle of the pituitary, but it is an important decomposition product of some unknown constituent. The extracts used in therapy contain histamin. The posterior lobe of the pituitary contains a hormone which is probably both blood-pressure raising and plain muscle stimulating. H. E. R.

Hirschfelder, A. D., Lundholm, A., and Norrgard, H. The local anaesthetic action of saligenin and other phenyl carbinols. *J. Pharmacol. & Exper. Therap.*, 1920, **15**, 261.

The anaesthetic action and toxicity of various phenyl carbinols were studied. Saligenin was found to be the most suitable, and records are given of operations performed on the human subject using saligenin as a local anaesthetic. H. E. R.

Abel, J. J., and Nagayama, T. On the presence of histamin in extracts of the posterior lobe of the pituitary gland and on preliminary experiments with the Pressor constituent. *J. Pharmacol. & Exper. Therap.*, 1920, **15**, 347.

The various methods for measuring blood-volume are discussed, and it is pointed out that measurements of haemoglobin or of plasma do not measure the volume of the blood but only of the constituent measured. Further, vasomotor and circulatory changes may simulate changes in blood-volume. The vital red method is the best method for measuring the volume of the circulating plasma, but the results should not be expressed in terms of total blood. H. E. R.

Aebly, J. Über Fehlerbestimmungen bei der viscosimetrischen Volumbestimmung der roten Blutkörperchen. [**Determination of the error in the viscosimetric measurement of the volume of the red corpuscles.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 1.

It is shown mathematically that the mean error in carrying out this determination by Ulmer's method is of the order of 3 per cent. when the corpuscular volume is in the neighbourhood of 50 per cent. But the absolute and relative mean errors rapidly increase with diminution of corpuscular volume, so that with very small corpuscular contents, as in pernicious anaemia, the results are unsatisfactory. C. L. E.

Jarisch, A. Über die Wirkung der Schilddrüse auf Kaulquappen. [**The effect of thyroid on tadpoles.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 159.

The author concludes that it is unnecessary to assume that the thyroid has any direct effect on development. Such effects as are seen in tadpoles are due to the fact that it accelerates metabolism, with the result that the larval organs are absorbed, and metamorphosis simulated. When given in one large dose, fatal effects may follow from the rapid absorption of the gills unless the larvae are kept in oxygen. C. L. E.

Gildemeister, M., u. **Kaufhold, R.** Über das elektrische Leitvermögen der überlebenden menschlichen Haut. [**The electrical conductivity of surviving human skin.**] *Arch. f. d. ges. Physiol.*, 1920, **179**, 154.

Although the electric current fatal to man is estimated by Boruttau at 400–500 milliamperes, the authors found that much smaller currents were able to pass through recently dead human bodies when a continuous current of 110–120 volts was applied, viz. only about 20–220 milliamperes. It was concluded that if the estimate of Boruttau is correct, the conductivity of the skin at the moment of closure of the current must be much greater than that measured in these experiments. C. L. E.

Höst, H. F., u. **Hatlehol, R.** Om blodsukkermængden og blodsukkermetoder. [**Tests for glucose in the blood.**] *Norsk Mag. f. Lægevidensk.*, 1920, **81**, 877–99.

Höst and Hatlehol have carried out 35 tests for glucose in the blood of 28 persons classified according as they were (1) healthy, (2) the subjects of diseases other than diabetes, and (3) diabetics. The tests compared were: (1) Bang's, recently modified by Bang and Hatlehol (*Biochem. Ztschr.*, 1918, **86**, 264), (2) Hagedorn and Normann Jensen's, (3) Myers and Bailey's (Benedict's), and (4) Folin and Wu's. The tests were controlled by examinations of blood to which a known quantity of glucose had been added. The differences shown in the amount of glucose, as indicated by the four different tests, were considerably greater among the diabetics than the persons in the other two classes. With one exception, the amount of glucose found in the blood of the 9 healthy and the 8 patients not suffering from diabetes was found by Bang's and Hagedorn's tests never to exceed 0·11 per cent. But Folin's method in these two classes indicated as much as 0·11 per cent. on two occasions, and Benedict's on three occasions gave figures between 0·11 and 0·12 per cent. In one case as high a figure as 0·142 per cent. was found. H. and H. doubt whether the tests hitherto devised for estimating the sugar content of the blood exclusively indicate its glucose content. Bang's and Hagedorn's tests gave more or less identical figures both for healthy persons and for diabetics. Folin and Wu's, and still more Myers and Bailey's modification of Lewis and Benedict's test, were apt to give too high figures in the subjects of diabetes with hyperglycaemia. C. L.

Jensen, C. O. Om standardisering af thyreoidea-præparater ved anvendelse af axolotl'er. [**Standardization of thyroid preparations on axolotls.**] *Hosp. Tid.*, 1920, **63**, 505–15.

Jensen considers that as thyroid preparations are much used, and their action can be harmful, their accurate standarization is imperative. The U.S.A. pharmacopoeia insists on a minimum of iodine in commercial preparations, although this does not constitute a reliable index to the potency of any thyroid preparation. A more accurate test would probably be quantitative estimations of metabolism in animals treated with various thyroid preparations, but no such tests appear to have been made. Jensen has investigated the effects of five different thyroid preparations on the development of the larvae of *Amblystoma mexicanum*, and, as his various tables show, these larvae react with sufficient uniformity to give a reliable criterion by which to judge of the specific action of any thyroid preparation. It was found that the ability of various preparations to promote metamorphosis of these larvae did not directly coincide with the iodine-content of the thyroid preparations. Thus, Vermehren's thyroidin proved most potent, although its iodine-content was ten times less than that of certain other thyroid preparations. C. L.

Widmark, E. M. P. **The kinetics of the ketonic decomposition of aceto-acetic acid.** *Acta med. Scandin.*, 1920, **53**, 393.

In the transformation of the acetone substances in the body, as well as in the separate estimation of acetone and aceto-acetic acid in body fluids, due regard must be paid to the reaction. The changes in reaction in the blood due to the severest conditions of acidosis will not measurably increase the velocity of the decomposition of aceto-acetic acid to acetone, but in the estimation of aceto-acetic acid in urine and blood care should be taken that the fluids are on the alkaline side of the neutral point. These views are based on a careful study of the reaction velocity of the change of aceto-acetic acid to acetone. C. G. L. W.

Geelmuyden, H. C. Über den Gehalt des Blutes an Fett und über den Gehalt der Leber an Fett und Glykogen im diabetischen Koma. [**The amount of fat in the blood and of fat and glycogen in the liver in diabetic coma.**] *Acta med. Scandin.*, 1920, **53**, 381.

Geelmuyden has examined the glycogen and fat-content of the liver and the fat-content of the blood in cases of diabetic coma, and as control has made a like examination in a certain number of non-diabetic cases. His object was to ascertain if a relation existed between the state of nutrition of the liver and the onset of coma. The percentage of glycogen in the liver varied from 0·06 to 3·02; fat from 2·63 to 7·32. The glycogen content of the liver of non-diabetic cases was from 0·66 to 0·20 per cent. There is no simple relation between liver glycogen and liver fat. The differences which are found between acute experimental diabetes and that taking place in man are to be explained by the difference in the velocity with which sugar is formed from fat in the liver. In human diabetes the pancreatic hormone is not removed so suddenly or so completely as when the pancreas is totally ablated. C. G. L. W.

Mahnert, A. Beiträge zum Studium der Veränderungen des Blutserum-Eiweissgehaltes unter verschiedenen Einwirkungen. [**The content of protein in blood-serum under different conditions.**] *Ztschr. f. physiol. Chem.*, 1920, **110**, 1.

The author has investigated the protein content of blood-serum in narcosis, after X-ray treatment, in pregnancy and in cases of tumour and chronic cachexias.

The values are lower than normal in narcosis and in X-ray treatment. The same is true in pregnancy, which is believed to be due to the increased blood-volume in these cases.

The protein is also diminished in carcinoma, but the test cannot be used for diagnostic purposes, as Tuffier and Maute have claimed, for certain cases of inoperable cancer have given amounts which were quite within normal limits. C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

Wilsey, R. B. **Tests of X-ray intensifying screens.** *Am. J. Roentgenol.*, 1920, **7**, 196.

Describes the results of tests carried out on the chief characteristics of intensifying screens, viz. speed (or intensifying factor), definition, and graininess. The photographic material used was 'dupli-tized' X-ray film, and the tests were carried out with a Coolidge radiator type tube running at a 5-inch gap and passing 10 milliampères.

With some screens the double combination was found to be faster than a single screen, while in other cases the single screen was faster. All screens gave better contrast when used as a double combination. The speed varied with the part radiographed, and for a double screen increased with the X-ray intensity.

Better definition was obtained with an unscreened than a screened film, and with a single screen than a double screen. Definition was found to be largely a function of the graininess of the screen. F. L. H.

Radiotherapy

Opitz, E. Sur les rayons X et du radium fortement filtrés. [**Highly filtered X-rays and radium.**] *Strahlentherap.*, 1919, **9**, 335. (*J. d. radiol. et d'électrol.*, 1920, **4**, 139.)

The author holds that Fribourg's method has never caused any accidents. The bases of this method are physical and biological.

Physical bases. Filtration with 16 mm. aluminium or 1 mm. copper. The radiation coming from a Coolidge tube filtered in this way is practically homogeneous. In thin persons ½ mm. copper or 10 mm. aluminium is sufficient. The focal distance employed is 60 cm. instead of 20 cm.; thus the loss by dispersion is greatly diminished. The size of the field of irradiation is of great importance. Krönig and Friedrich have demonstrated that the quantity of secondary rays whose action is added to that of the primary beam depends within certain limits upon the size of the area irradiated. For large areas, 15 cm. × 13 cm., the secondary irradiation becomes much greater, and at a depth of 8 cm. the dose is three times that given by calculation. It is for this reason that, for deep therapy of uterine fibroids, two areas of 15 cm. by 15 cm. were chosen: one dorsal and one ventral.

Biological bases. The laws of biological action of the rays are summed up, according to Krönig's and Friedrich's experimental researches, in the following propositions:

1. The biological action of the rays depends on the quantity of rays absorbed by the tissues.

2. This action is (within wide limits) independent of the hardness of the rays.

3. Action is more powerful if the dose be administered at one time than if it be split up.

4. Action is stronger, with a stronger intensity of irradiation in unit time.

In practice, therefore, it is best to apply the whole dose in one séance with the maximum intensity.

Dosage. The measurements are made with an ionization apparatus. The author uses as unit of measure the unit *e*, introduced by Friedrich and defined as follows: The quantity of rays necessary to produce by ionization in 1 c.c. of air, a quantity of electricity equal to an electrostatic unit (one unit X would correspond to 3 units *e*).

The cutaneous or erythema dose is 170 *e* and gives rise to a slight redness of the skin. It should not be renewed before 6 months. The ovarial dose has been fixed by Krönig at 35 *e*, i.e. at $\frac{1}{5}$ of the cutaneous dose. The carcinoma dose is 150 *e*. S. U. L.-B.

Delbet, M. P. Fibromes utérins et radiothérapie. [**Uterine fibroids and radiotherapy.**] *Bull. et mém. Soc. de chir.*, 1920, March. (*Arch. d'électric. méd.*, 1920, **28**, 158.)

The author, in the course of a discussion at the Société de Chirurgie quoted an observation of Kotzareff: The patient, 44, with the myoma giving rise to severe metrorrhagia, was treated in Switzerland by radiotherapy. After the third séance, excessive haemorrhage supervened, weakening the patient considerably. Subtotal hysterectomy was performed a fortnight later. The extensive haemorrhage might have given rise to a suspicion of malignant change consequent upon the radiotherapy, but anatomo-pathological examination of the mass removed showed that it consisted of a congenital tumour, an adenomyoma, and consequently a malformation, not a cancer. Baudet declared that he would never willingly use radiotherapy for uterine fibroids, holding that it does not completely cure a fibroid, that it runs the risk of sterilizing the ovaries, and provokes an early menopause; that it leaves other morbid diseases in a fibroid, as bad as or worse than itself. In 130 surgical operations Baudet had only 4 deaths, and of these 130 cases 100 were complicated by incarceration, pregnancy, torsion, prolapse, &c., and the remaining 30 were simple fibromyomata, for which he maintained that radiotherapy is neither completely nor definitely efficacious. Radiotherapy should not be used in these last cases unless there are indications against intervention. Baudet considered such cases to be the only ones justifying the new treatment. Delbet concluded from the discussion that radiotherapy does not cure 99 per cent. of fibroids, as was indicated by Béclère's statistics. The radiologists' percentages are relative to selected cases. Many patients, tired of radiotherapy, go to the surgeon without informing the radiologist, who believes them to be cured.

Souligoux and Chifoliau rejected radiotherapy systematically. The former asserted that the rays act on the suprarenal capsules, but many spleens and uteri have been irradiated without injury to the intestine; the rays can be focussed accurately and the danger seems too hypothetical for such summary rejection of radiotherapy for fibroids. Chifoliau rejected it on the grounds that he considers hysterectomy to be less serious than irradiation. Delbet did not agree with this, as no uterine accidents have been reported which were ascribable to irradiation. However, Mornard's cases of fibroids remained, in which 3 out of 32 that had been treated by radiotherapy were complicated by very rapid development of cancer. There are no grounds for affirming that irradiation caused the cancerous growths, but there can be hardly any doubt that it accelerated their development. The argument of conservation of fertility is worked both by the surgeons and the radiologists, but preservation of the ovaries and of the uterus after radiotherapy is very uncertain and cannot be depended upon. In all cases, unless diagnosis of fibroid is certain, laparotomy is preferable to radiotherapy. If there are associated injuries, operation is best, but it is very difficult to draw any indication or counter-indication from the fibroid itself. This is the crucial point of the whole question, yet less light was thrown on it than on any other point in the discussion. (1) The structure of the fibroid and its state of evolution and (2) its topography should be kept in mind.

(1) Calcified fibroids; those in ischaemic degeneration; gangrenous fibroids; those complicated by blood or pus in the uterus; those which develop rapidly after the menopause; lymphangiectatic and cystic fibroids are all suitable for operation. The composition of the tissue should be taken into account. Muscular tissue is less affected by X-rays than connective tissue. This is the reason why there is no result from radiotherapy of adenomyoma. In diffuse hypertrophy which appears to be due to adenomyomatosis one must rather lean towards operation.

(2) Pedunculated subperitoneal fibroids and pedunculated submucous fibroids that can be removed through the vagina, with preservation of the uterus, are amenable to operation. In the case of incarcerated pelvic fibroids and those which have ascended above the brim of the pelvis and are often easily extirpated, it is a question of temperament and of the individual case.

Belot holds that it is best not to irradiate fibroids larger than a child's head because there always remains a large tumour which causes trouble. Small and medium-sized fibroids will benefit by radiotherapy and with the exception of pure myomata and adenomyomata, the majority of fibroids pass through a phase amenable to irradiation. Also, patients whose general condition is against operation will derive benefit from irradiation. Hence the author considers that, although contra-indications to radiotherapy are numerous, they do not amount to prohibition. Indeed, in spite of uncertainties, radiotherapy for fibroids can be of great use. Nevertheless, he believes that in the future radium therapy will take the place of X-rays.

S. U. L.-B.

British Medical Association. Joint discussion on the treatment of uterine fibroids. *Brit. M. J.*, 1920, ii, 535.

The following were the views expressed during a discussion on the treatment of uterine fibroids at the meeting of the British Medical Association held at Cambridge, June 30–July 2, 1920. Robert Knox pointed to the necessity of close co-operation between gynaecologist and radiologist in the treatment of fibroids. He laid stress on the importance of blood-counts during treatment, a drop in the total leucocytic indicating its suspension, or continuance with caution. At first, most of the results of radiological treatment were presumably those produced by relatively small doses of X-rays. At present, the advent of the Coolidge tube has increased the possibility of administering fairly large doses at a considerable depth from the surface of the body. The action of the rays appears to be exerted primarily on the ovary and its blood-supply; the tumour also diminishes in size in a number of cases. It is not necessary here to refer to the details of treatment, but Knox gives a full description of the filtration, seats of irradiation and other points which he had found useful; and similar technical details were given by other speakers.

Haemorrhage generally ceases after the third séance, but the biological reaction of individuals is not uniform; some patients respond more readily to small doses, others to larger doses at longer intervals. Certain coexisting conditions contra-indicate radiological treatment, such as degeneration with or without calcification; pelvic infection and suppuration; inflammation of neighbouring organs; submucous pedunculated fibroids. The advantages are, painless treatment not disturbing the patient's ordinary life; no elaborate preparations; the severe nervous disturbances and shock are obviated in the resulting menopause.

The disadvantages are, the length of time to effect a result; the facts that radiotherapy is not always successful, that the tumour remains though greatly reduced, and that unfavourable changes may occur in the blood.

Immediate effects are nausea, headache, and giddiness; later effects appear several days after treatment and vary according to the dose, a heavy dose sometimes being followed by general malaise.

Interstitial fibroids derive the greatest benefit, but practically all forms of fibroid, in patients of all ages, respond favourably to X-ray treatment unless symptoms show the need of immediate operation. The advantages of radium over X-rays must be considered. Radium can be brought to the bedside and the dose can be more accurately estimated.

Herbert Williamson said that by no means all fibromyomata are suitable for X-rays. He would limit the treatment to cases over forty years, with small tumours showing no degeneration or inflammatory changes, no malignancy, or anaemia. X-rays are of value in the treatment of 'chronic metritis', but curettage should be done to exclude carcinoma of the body. He appealed for uniformity in dosage, and clear statements on methods of application, so that the treatment could be placed on a scientific basis.

Louisa Martindale had employed X-ray treatment in thirty-seven out of ninety-three cases, physical signs and symptoms being the determining factors. If the tumour were interstitial, did not exceed the size of a six months' pregnancy, and if menorrhagia were the prominent symptom, X-ray treatment was chosen. The same was the case if the patient had serious heart disease; often, subsequent to treatment, recovery took place from the profound anaemia induced by the repeated haemorrhages. Diminution in size of the tumour appears gradually and continues long after cessation of treatment. In most cases there are no unpleasant effects. In her opinion it was the best treatment for a straightforward case. The treatment takes several hours, two to three hours with a Coolidge tube, and is carried out on two consecutive days and continued after an interval of seventeen to twenty-one days, irrespective of menstruation.

Cuthbert Lockyer said that radiotherapy acts mainly by destroying the ovaries, but X-rays also have a destructive influence on the myoma, as evidenced by the coincident shrinkage. Radium and mesothorium alone are not as suitable as X-rays for cases of myoma, but combined with X-rays appear to effect more rapid haemostasis. The French 'cross-fire' combined with intensive technique, promises the best results.

He did not agree with those authors who considered no age a bar to treatment. The technique was not sufficiently exact to justify the use of rays in a young subject; it is first necessary to have a regulated dosage, to ensure normal menstruation following on treatment. He urged that a standard measurement of dosage was necessary, to ensure close co-operation between surgeons and radiologists.

F. L. Provis said that X-ray treatment was of the highest value in properly selected cases in women over thirty-eight years of age. The medium-sized interstitial fibroids were those most successfully treated. He thought it impossible for the treatment to produce amenorrhoea without upsetting the internal secretion of the ovary, so advised operation in young patients.

Agnes Savill advised fewer exposures and shorter doses to avoid X-ray sickness.

William Mitchell considered that the question of dosage and duration of treatment should rest with the radiologist, and that exact statements should be given as to amount and frequency of dosage.

Gilbert Scott said it was essential that the gynaecologist and the radiologist should collaborate, and that satisfactory results were dependent on efficient dosage and careful investigation of the case before treatment.

Florence Stoney, after giving details of eight cases of fibroids cured by X-rays, insisted that any bad results should be published, and that post-mortem and post-operative findings after irradiation should be recorded.

Shillington Scales agreed that our present methods of treatment were largely empirical, and as these methods differed so considerably in detail (though arriving at the same result) it was impossible to lay down an accepted standard at the present time. S. E. P.

TUFFIER, FREDET, FAURE, et HARTMANN. Cancers à évolution extrêmement rapide greffés sur des fibromes utérins au cours de leur traitement par la radiothérapie. [**Very rapidly developing cancers grafted on uterine fibroids in the course of their treatment by radiotherapy.**] *Bull. et mém. Soc. de chir.*, 1920, January. (*Arch. d'électric. méd.*, 1920, **28**, 216.)

Tuffier only followed the cases of two patients treated by X-rays for fibroid. The first, after operation, showed no modification, either of the uterus or of the tissue of the tumour. The other, which was as large as an orange, developed gradually and was treated by X-rays. The tumour diminished, menstruation ceased, and afterwards recommenced. Fifteen months later the patient lost so much that she requested surgical intervention. The fibroid was then the size of the foetal head. Tuffier recommended further séances until menstruation should have ceased. In his opinion, sarcomatous changes and epitheliomata of the uterine cervix and body are not rare in cases of fibroid. Possibly the frequency of the radiotherapeutic séances plays a part in this. Summing up his views, he held that results of observations seem to show that menstruation can be conserved after irradiation of the fibroid, but destruction or preservation of the ovary cannot be predicted. In cases of small fibroids it seems impossible to be certain that the ovary, has not been included in the irradiated area. Destruction of the ovary, if it is not the aim of the treatment, is an almost inevitable complication. Although X-rays may be acceptable in the cases of multiple and very large fibroids, it is otherwise in cases where fibroids are few or single, especially in young women who can be treated by myectomy.

Out of 121 cases Fredet observed 65 simple fibroids and 56 which were associated with important lesions (ovarian cysts, cysts of the broad ligament, salpingitis, umbilical hernia, adherent omentum, sclero-cystic ovaritis, appendicitis, hematomata). Consequently, in more than two-fifths of the cases, radiotherapy, if it had been applied, would have left lesions which in all probability it could not cure. Therefore it may be said that at least one-third of the fibroids for which the surgeon is consulted justify laparotomy. If radiotherapy really does all that is asserted, patients with haemorrhagic myomata, who bear anaesthetics badly, would derive the greatest benefit from its use. Faure considered surgery to be superior to any other treatment. It will cure 95 per cent. of fibroids, while X-rays cures many, but loses, through various accidents, a greater number, and even in the cases of cure, the result is less satisfactory than that obtained by surgical intervention. In 100 cases treated by radiotherapy he saw no serious accident. He observed a case similar to one of Mornard's, in which a tumour, at first diagnosed as fibroid, rapidly presented the appearance of a cancer. Only one séance had been held and this could not have been sufficient to change an old fibroid into a cancer. At the time when the rays were applied, the neoplasm was certainly already in existence, and one wonders if the same was not the case in Mornard's three cases.

In most of Faure's cases there was marked improvement from the application of X-rays: disappearance of haemorrhage, then of menorrhagia, suppression of the periods in the third month, decrease in the size of the tumour, except when this was too large.

The mechanism of cure still remains unknown. It is possible that it acts on the ovaries, although normal ovules have been found in irradiated ovaries. If the uterus only be acted upon it seems difficult to avoid irradiating the ovaries, since it is impossible to ascertain their position. For the last two years Faure has substituted radium therapy for radiotherapy in his treatment of fibroids. All the cases thus treated were cured, whether by radium alone, or in conjunction with X-rays. 30 patients were treated by radium alone and the action was immediate. One application was nearly always enough. Haemorrhage ceased, the periods did not recur, and the fibroid began to decrease in size. Some of the patients were seen later with the uterus normal.

It is certain that treatment by X-rays and by radium are very serious and efficacious methods, not to be passed by on the pretext that they give rise to failures and accidents.

At the same time, certain cases should be operated upon: those in which diagnosis is doubtful, rapidly developing fibroids, cases with pelvic inflammation, with necrosis or infection of the fibroid. Operation should also be performed in cases of fibroid co-existent with pregnancy, very large fibroids, fibroids with multiple hard fibrous centres, and especially when a neoplastic degeneration of the uterine mucosa is suspected. Hartmann remarked that intra-uterine cancers are frequently co-existent with fibroids. There is, therefore, considerable danger in treating them by X-rays. Radiotherapists constantly believe that they have excellent results because the patients do not come to see them if an accident occurs. In a case of apparent recurrence there was a cystic endometritis which recalled the lesion observed in the tubo-uterine duct of a sow previously submitted to prolonged applications of X-rays. Hartmann, like Souligoux, had observed several cases in which radiotherapy was followed by a state of absolute emaciation. In one case a woman of 41 appeared as if mummified. He also preferred the action of radium to that of X-rays. S. U. L-B.

Quénu, E. Cancers à évolution extrêmement rapide. [**Rapidly developing cancers.**] *Bull. et mém. Soc. de chir.*, 1919, December. (*Arch. d'électric. méd.*, 1920, **28**, 255.)

Resuming the question of radiotherapy for fibroids, raised by Delbet at the Société de Chirurgie, the author is of the opinion that certain types of fibroids should not be treated by radiotherapy; not only fibroids undergoing ischaemic degeneration, but also those which have become calcified, and those in which there is a suspicion of epithelial degeneration of the endometrium. To these must be added the cases in which the adnexa are inflamed or the seat of new growth, small fibroids complicated by uterine prolapse or by pyometra and those complicated by pregnancy (although the author quotes a case of pregnancy brought normally to term after nine irradiations).

He followed the cases of three patients with fibroids who were treated by radiotherapy. All three, after undergoing treatment for two years, had to resort to surgical intervention, the first on account of the return of haemorrhage, the two others because of redevelopment of the tumour. After radiotherapy, the tumours having decreased in size, it is possible that the radiotherapist counted them as cures. A striking coincidence was the appearance during treatment of cancer of the breast in two of the patients. The author does not consider the radiotherapy to have been responsible, as he frequently observed the co-existence of uterine myoma and tumours of the breast, often malignant. Besides, he had frequently noticed that patients with fibroids showed epithelioma of the endometrium of the corpus uteri. Hence X-rays, if not actually causing epithelioma, may affect the development of an already existing cancer. Even if it had no ill effect, radiotherapy would have this evil consequence, that it would deflect the patient from the only safe course, i. e. surgery. Thiéry did not think that in Mornard's cases, reported by Delbet at the discussion, epithelioma was produced by radiotherapy, but considered that without doubt the extraordinarily rapid development must be ascribed to the X-rays, which are harmful in deep cancers.

Routier had operated on a large number of cases which had previously been treated unsuccessfully by radiotherapy. In the case of a patient with an enormous fibroid which had been treated for twelve or thirteen years by radiotherapy, he found, on operating, a doubtful uterine cavity; eleven months later, the patient died of generalized carcinoma. He considered that radical removal of the tumour is better than any electrical treatment.

Souligoux did not believe that exact localization of the action of the rays on the ovaries is possible; outside the area the rays might affect essential glands such as the suprarenal capsules and the pancreas. In the case of a patient with a small fibroid treated by radiotherapy, the tumour decreased, but the patient, formerly in good health, became gradually thinner, and died in a state of absolute emaciation. S U. L.-B.

Aubourg, P. A propos du traitement de certaines radiodermites chroniques professionnelles par les applications de neige carboniques. [**Treatment of a chronic dermatitis in a professional radiologist by means of carbonic acid snow.**] *J. de radiol. et d'électrol.*, 1919, **3**, 217.

A. reports the result of treatment of a chronic dermatitis in a professional radiologist by means of carbonic acid snow. The subject is of special interest in that the condition occurred in a radiologist who, during an experience of thirteen years, took all available precautions against the injurious action of X-rays. Two years previous to the outbreak of war chronic lesions appeared on both hands, especially on the dorsal surface of the left hand. The large amount of screen work necessitated by the localization of foreign bodies among the wounded aggravated the condition of the lesions, which had now become so numerous that treatment was necessary. A feature of great interest was that there was no appreciable departure from the normal in blood-counts of the patient. The lesions were of two kinds, one an exuberant type of over-growth, painful under pressure, sometimes bleeding; the other type was an ulcerous type, also very painful. The same treatment was carried out for all of the lesions, numbering 23 ; carbon dioxide snow was applied to the surface for 40 seconds, immediately after which the surface was covered over with a preparation of bismuth subnitrate, which was kept continuously in contact for 10 to 15 days. In 21 of the lesions the healing was complete; in the remaining two suppuration occurred in one which cleared up under treatment with magnesium chloride ; the other recurred three months after treatment, but this was successfully removed. One year from the commencement of the treatment the hands of the patient were in such a good condition that hardly any traces of the lesions were visible. The report ends with a note of warning as to the necessity for rigorous measures of protection in all forms of X-ray work.

S. R.

MEDICAL SCIENCE

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REVIEWS

SYPHILIS

Aetiology. The history of scrofula is associated with that of tuberculosis, and more recently with that of syphilis, more especially inherited syphilis. After the discovery of the tubercle bacillus, the old scrofula was generally regarded as a form of tuberculosis. Some clinicians, however, struck by the resemblance of so-called scrofulous lesions to certain lesions occurring in the course of syphilis, concluded that there was an aetiological relationship between syphilis and scrofula. At any rate, it must be admitted that a number of lesions formerly regarded as scrofulous are now known to belong to inherited syphilis.

The question whether anything remains of the old scrofula, after scrofulo-tuberculosis and scrofuloid syphilis have been withdrawn, is discussed by Sergent, who is of opinion that the term scrofula should be preserved. He classifies scrofula as follows: (1) scrofula proper, represented by the first stage of the scrofula of the older authors; (2) scrofulo-tuberculosis, which includes most of the manifestations of the more advanced stages of the old scrofula; (3) syphilo-scrofula, which consists of hybrid lesions of syphilis and tuberculosis, and must be distinguished from scrofuloid forms of syphilis.

According to Sergent, the first class, or **scrofula proper,** is manifested by chronic inflammation of the nasopharynx, leading to adenitis, adenoid vegetations, hypertrophy of the tonsils, and pharyngeal tonsil, and hypertrophic rhinitis, and secondary effects such as otitis media, and mastoiditis, conjunctivitis, blepharitis, dacryocystitis, phlyctenular keratitis, and frontal sinusitis. Irritation of the skin by the nasal discharge causes chronic impetigo and eczema, resulting in hypertrophy of the upper lip, which, with swelling of the nose due to chronic rhinitis, gives rise to the characteristic strumous facies. Most of these cases come into the category of 'lymphatics'. **Scrofulo-tuberculosis** corresponds to malignant scrofula of the older authors and includes lesions which are definitely tuberculous, such as lupus and other forms of cutaneous tuberculosis, and tuberculous adenitis of the cervical and other glands. In **syphilo-scrofula,** constituted by a symbiosis of syphilis and tuberculosis, there may be an hybridity of soil or an hybridity of lesions. In the former, syphilis acts as a predisposing cause of tuberculosis; in the latter, there is a combination of syphilitic and tuberculous lesions. Sergent points out that it is difficult to establish any distinct demarcation between these two types, and that probably there is always an hybridity of the soils with more or less intricate juxtaposition of lesions. The best example of this condition is the hybrid of lupus and syphilis, in which part of the lesion heals under antisyphilitic treatment, while the tuberculous part remains.

With regard to the differential diagnosis between the three types, as Sergent remarks, in the majority of cases it is easy to distinguish cervical adenitis due to adenoids from scrofulo-tuberculous adenitis, but the diagnosis between scrofulo-tuberculosis and syphilis is more difficult. Syphilis may simulate tuberculosis (scrofuloid-syphilis) or be associated with it (syphilo-scrofula). Syphilis and tuberculosis may manifest themselves by lesions of identical localization and similar aspect. This is true, not only for inherited syphilis, but also for the acquired disease. In these cases the diagnosis depends to a great extent on the presence of other signs of syphilis, the Wassermann reaction, and the therapeutic test. The association of the two diseases complicates the problem. The only absolute proof of the tuberculous nature of a lesion is the presence of the bacillus of Koch. The Wassermann and tuberculin reactions only give evidence of the nature of the soil, not of the nature of the lesion. The beneficial effect of antisyphilitic treatment is not conclusive and does not prove the absence of tuberculosis, for it has been shown that the tuberculosis of syphilitics is generally improved by antisyphilitic treatment.

As regards the prognosis of these types, the first type, or scrofula proper, represents a condition which is predisposed to tuberculous infection; in which case it is transformed into the second type, or scrofulo-tuberculosis. Again, in the opinion of Sergent, Gaucher, and others, the 'strumous' subjects belonging to the first type are the children of syphilitics. The syphilization of the parents prepares the soil for the tuberculization of the children. The prognosis, therefore, depends, to a great extent, on early treatment.

Concerning treatment, apart from general hygienic measures and local treatment, it is essential to institute antisyphilitic treatment if there is any sign of syphilis or even a suspicion of syphilitic antecedents.

Symptomatology. A case of **reinfection,** after a single course of '606', is reported by Vallery-Radot. The patient presented a typical indurated chancre of the coronal sulcus with characteristic adenopathy. The *S. pallida* was found and the Wassermann reaction was positive. Five years previously he had been treated for primary and secondary syphilis with four intravenous injections of '606'. On this occasion there were two chancres, both in different situations to that of the chancre of reinfection. The Wassermann reaction had remained negative on several occasions and no further symptoms developed. This appears to be undoubtedly a genuine case of reinfection, and shows that syphilis may sometimes be cured by a single course of arsenobenzol.

Léri and Cochez report two cases of **buccal pigmentation** in old syphilitics. In the first case, a man aged 52, there were numerous brown spots on the mucous membrane of the cheeks, lips, and palate, but no pigmentation of the skin. There were no signs of Addison's disease or any of the usual conditions which would account for the pigmentation. There was a history of a chancre in youth, and an X-ray examination showed bulging of the aorta, which was regarded as syphilitic, although the Wassermann reaction was negative.

In the second case, a woman aged 71, there were similar, but smaller, spots in the buccal cavity and also vitiligo of the skin. This patient was definitely syphilitic, with signs of tabes and sclero-gummatous glossitis, and a positive Wassermann reaction.

The authors regard the buccal pigmentation as syphilitic in origin, a form of vitiligo of the mucous membrane, in both these cases, and are of opinion that many cases of so-called physiological pigmentation of the buccal mucous membrane are probably of the same nature. As regards the aetiology of this pigmentation, they favour Darier's view, that it is due to changes in the nerve plexus of the suprarenal glands caused by syphilis.

Two cases in which **gastric syphilis** assumed the form of chronic gastritis or dyspepsia are reported by Florand and Gérault. In the first case, a man aged 52, gastric pain and vomiting five hours after food had occurred continuously for six months. There was evidence of syphilis, but the Wassermann reaction was negative. The symptoms disappeared after four injections of arsenobenzol.

The second patient, aged 47, had suffered from chronic dyspepsia for four years. There was a history of syphilitic infection at the age of 24, and the Wassermann reaction was positive. This case improved with antisyphilitic treatment.

The authors remark that chronic gastritis is one of the forms in which gastric syphilis is manifested, and those cases which do not improve under the usual forms of treatment should be investigated for syphilis.

Berghausen reports two cases in which **lymphosarcoma** occurred in syphilitic patients. In the first case there was general enlargement of the lymphatic glands and also of the spleen. In the second case the adenopathy chiefly affected the cervical glands. Sections obtained before death showed the characteristic appearances of lymphosarcoma in the first case, and of Hodgkin's disease in the second case. The Wassermann reaction was positive in both cases. Antisyphilitic treatment caused only slight temporary improvement. The author is of opinion that the occurrence of lymphosarcoma in a syphilitic patient was a coincidence, and does not attribute any aetiological relationship to syphilis.

Bock reports that in 9,690 autopsies at the Rudolf-Virchow Hospital, Berlin, there were 385 cases of **aortic syphilis,** or nearly 4 per cent. In 173 cases in which the diagnosis of aortic syphilis was confirmed by autopsy, the Wassermann reaction was only positive in 66 per cent. Thus a third of the cases gave a negative reaction. Bock warns against attaching too great importance to a negative reaction in such cases and thereby neglecting the beneficial influence of treatment. The effect of antisyphilitic treatment in syphilitic aortic disease with regurgitation depends on the degree of compensation. Cases in which the compensation is not much impaired are most benefited by treatment. The treatment recommended by Bock consists in a preliminary course of mercurial inunction followed by injections of neosalvarsan 0·3 grm. twice weekly, and lastly iodide of potassium. In the case of deficient circulation and a tendency to oedema, a pill containing digitalis and mercury should be given till compensation is established, and then the course of mercurial inunction and neosalvarsan.

Oddo and Mattei report a fatal case of **pericarditis** which they consider to have been of syphilitic origin. The patient, a man aged 52, with secondary syphilis of the mouth and genitals, and a positive Wassermann reaction, had an attack of dyspnoea with cyanosis and signs of pericarditis. Temporary improvement occurred after intravenous injections of cyanide of mercury, but death took place from pulmonary oedema after four injections of novarsenobenzol. The autopsy showed perivascular infiltration of the pericardium with plasma cells, recent syphilitic disease of the coronary artery, and also old atheroma. The authors regard the case as one of syphilitic pericarditis, and remark that secondary syphilis of the heart is more common than is usually supposed. They consider that the treatment should be mercurial, and that arsenical treatment is dangerous and liable to cause syncope and pulmonary oedema, as in the above case.

In most text-books **renal syphilis** receives but little attention, and many writers have attributed the renal symptoms occurring in syphilis to the effects of mercurial treatment. Loyd Thompson considers that acute syphilitic nephritis is rare, and that Osler's estimate of 3·8 per cent. is too high. This condition must be distinguished from the transient albuminuria often met with in early syphilis, which is comparable to that of other infections. Acute syphilitic nephritis presents the same clinical symptoms as acute nephritis of non-syphilitic origin, but is characterized by the large amount of albumin. The kidney is of the large white type. The *S. pallida* has been found in the kidney in fatal cases, and Hoffmann found it in the urine. The diagnosis is sometimes difficult, as the cutaneous eruptions may be masked by oedema; also acute nephritis due to other causes may occur in a syphilitic subject. The presence of a spirochaete in the urine is not conclusive unless obtained by catheterization of the ureters. Acute syphilitic nephritis generally develops in the first six months of the disease. The renal function is less impaired than in other forms of acute nephritis.

Chronic syphilitic nephritis may be interstitial or parenchymatous, and appears after the third year. Diagnosis may be difficult, but if more cases of chronic nephritis were examined for syphilis, in Thompson's opinion, this would be more frequently discovered. A case improving under antisyphilitic treatment suggests a syphilitic origin.

A gumma of the kidney may simulate renal calculus or malignant disease. Sometimes the kidney is affected by a sclero-gummatous process. Amyloid disease of the kidney may occur as the result of prolonged toxaemia.

The prognosis of renal syphilis is better than those of other forms of nephritis, and most cases react well to treatment. In the acute form, treatment should be directed both against the nephritis and the causative disease; the nephritis being treated by digitalis, diuretics, cathartics, and the usual treatment for acute nephritis; the syphilis by small doses of neosalvarsan, 0·1 to 0·2 grm. at weekly intervals. Mercury should be withheld till the albumin has subsided. In chronic cases, arsenical and mercurial treatment should be pushed, after the diagnosis is confirmed by improvement after a small dose of neosalvarsan.

Copelli reports a case of acute syphilitic nephritis, occurring in the fourth month of syphilis, which was fatal from uraemia. Microscopical examination showed the presence of spirochaetes in the epithelium of the tubules, in the glomeruli, and also in the interstitial tissue and adventitia of the vessels. They were not found in the urine.

Judging by the literature, **prostatic syphilis** appears to be rare. According to Loyd Thompson only 24 cases have been recorded, only 12 of which can be accepted as syphilitic, including a personal case. The usual condition reported was either general or unilateral enlargement, but in only two cases were post-mortem findings recorded. The symptoms were pain during micturition, defaecation, and coitus, and the presence of pus and red blood cells in the urine. The diagnosis, therefore, depends on the presence of other signs of syphilis and the Wassermann test. The case observed by Thompson was in a man aged 39, with a history of chancre about 15 years previously. On examination his Wassermann reaction was positive, and he complained of dysuria. The right lobe of the prostate was enlarged, tender, and nodular.

The secretion obtained by prostatic massage was of a brown colour and negative for gonococci. After a course of treatment by injections of benzoate of mercury and salvarsan the prostate was reduced to normal size and the dysuria disappeared.

Marshall and Evans report a case of **syphilitic spondylitis** affecting the lumbar vertebrae, in a man aged 35, nine years after infection. A radiograph showed new bone formation around the second and third lumbar vertebrae, which were ankylosed by bridges of new bone over the intervertebral cartilages. A noteworthy feature in this case was the persistently negative Wassermann reaction, even during the development of the lumbar symptoms, and nodes on the clavicle and tibia. The symptoms, including signs of early cerebral meningitis, subsided after energetic treatment with mercurial inunction, potassium iodide, and salvarsan, leaving only rigidity of the lumbar spine. This case resembles one reported by Fournier in its localization in the lumbar vertebrae, but differs in the absence of suppurative osteitis, which was present in Fournier's case, and resulted in double psoas abscess.

The pathology of the **trophic lesions of tabes** has by some been attributed to disorders of the trophic action of the nervous system, by others to local disturbance independent of the nervous system. Achard and Rouillard report a case of perforating ulcer of the foot in a patient with no signs of tabes, which supports the latter theory. The patient, a woman aged 42, suffering from pulmonary tuberculosis, presented an ulcer on the sole of the right foot, with all the appearances of perforating ulcer. There were no signs of tabes, and the cerebrospinal fluid was negative. The Wassermann reaction in the blood, however, was positive, and there was a history of one still-birth and several early infantile deaths among the pregnancies. Three injections of arsenobenzol had no effect on the ulcer. The authors remark that perforating ulcer may occur in other diseases than tabes, as the result of lesions of the central or peripheral nerves; but that in the case of a syphilitic the future development of tabes is possible.

In the infirmary attached to 'De Gamles By', Vedsmand has examined for syphilis all the 84 cases of **hemiplegia** occurring between October 1919 and February 1920. Wassermann's reaction was positive in 13 cases, and in 2 others in which it was negative, and in which the cerebrospinal fluid was normal, the Argyll Robertson symptom-complex established the diagnosis of syphilis. Thus there were 15, or 17·9 per cent., that were syphilitic. Comparing his results with those of Henry A. Thomas, who studied the incidence of syphilis in 740 cases of hemiplegia, Vedsmand notes that his own observations shew a higher proportion of syphilitics. But he admits that the syphilitic infection may, in some of his cases, have played little or no part in provoking hemiplegia. Thus, one of his patients suffered from chronic nephritis and high blood-pressure. But in 5 cases he is sure that the syphilis was the primary cause of the hemiplegia. Among the remainder the relation of the two conditions was more questionable.

The rôle played by syphilis in affections of the **glands of internal secretion** has of late received increasing attention. In a summary of our present knowledge of this subject, Schulmann first of all points out that these glands, by reason of their vascularity, are especially vulnerable to syphilitic infection, and that their glandular cells form a suitable nidus for the multiplication of spirochaetes.

The connexion between syphilis and disease of the endocrine glands appears to have been first suggested by the frequent co-existence of exophthalmic goitre with tabes. The demonstration of *S. pallida* in these glands, by Jacquet and Sézary, and the frequent occurrence of a positive Wassermann reaction in endocrinic diseases, gave further evidence of the syphilitic factor in these cases. The affinity of *S. pallida* for the *suprarenal capsules* has been known for some time. In inherited syphilis lesions of these organs are nearly as common as those of the liver and spleen, and, according to Sézary, when the subjects survive, these organs are left in a state of functional meiopragia and susceptible to complications on the occasion of any infection. In acquired syphilis the suprarenals are less often affected, but symptoms of Addison's disease have been several times noted in the course of secondary and tertiary syphilis; the first case being reported by Gaucher in 1880. The pigmentary syphilide has also been attributed to lesions of these glands. The administration of adrenalin as a remedy in cases of accidents after the injection of arsenobenzol compounds, introduced by Milian, is based on this connexion, and it has been suggested that these accidents occur more especially in subjects in whom there is suprarenal insufficiency.

The *thyroid gland* is more often affected in acquired than inherited syphilis in the form of secondary thyroiditis and gummatous or sclero-gummatous processes. In the event of the parenchymatous cells being affected, one of two conditions may result: hyposecretion with symptoms of myxoedema; hypersecretion which has been alleged as a cause of exophthalmic goitre. According to Schulmann, exophthalmic goitre may develop at any period in the course of acquired or hereditary syphilis, and he mentions a case of Strumpke's which developed in the early secondary stage and was cured by salvarsan.

The *pituitary gland* may be affected both in acquired and hereditary syphilis, either by direct infection, or less often by extension from a basal meningitis. The clinical symptoms vary according to the portion of the gland affected. Lesions of the posterior and intermediate portions of the gland appear to be responsible for glycosuria and diabetes insipidus. Schulmann mentions a case of this kind in which gummata were found in the posterior lobe at autopsy. Hypersecretion of the pituitary gland may give rise to acromegaly, the syphilitic origin of which has been affirmed by several observers. Diminished function of the gland has been alleged as a cause of Fröhlich's adiposo-genital syndrome and of osteitis deformans.

With regard to the *pineal gland*, the *parathyroid glands*, and the *thymus* there is less evidence of syphilitic infection, but gummata have been reported in the latter, and myasthenia has been attributed to disease of the thymus in old syphilitics.

Syphilis of the *pancreas* is not infrequently associated with symptoms of diabetes, which may occur during the secondary or tertiary stages. Cases in which these symptoms were caused by antisyphilitic treatment have been recorded. In hereditary syphilis, according to Fanoy, the defensive reaction causes increase in the islands of Langerhans, and transforms the pancreas into an endocrinic gland, which explains the comparative rarity of diabetes in the subjects of hereditary syphilis, in spite of the frequency of syphilitic lesions of the pancreas.

With regard to the *testicle*, apart from disturbances in the function of spermatogenesis caused by syphilitic orchitis or epididymitis, the internal secretion of the gland may be altered. The effects of this alteration are not well known, but cases of arrested development of the secondary sexual characters have been reported. The same applies to syphilis of the *ovary*.

In the case of the testicle and ovary the results of altered internal secretion are complicated by the effects on other glands. Functional synchronism appears to be the rule in endocrinology, so that those glands are not to be regarded as isolated organs, but rather as different factors in a complex system. Among other dystrophic conditions which have been attributed to the effects of syphilis are dwarfism and giantism, infantilism, osteomalacia, and achondroplasia. In Schulmann's opinion, the cause of all these dystrophies lies in disturbance of the endocrine glands, and the toxinic syphilis of the older authors is generally endocrinic heredo-syphilis.

As regards the treatment of endocrinic syphilis, antisyphilitic treatment by arsenic, mercury, and iodides should be combined with opotherapy. Caution in arsenical treatment is necessary in the case of suprarenal disease.

Feit remarks that disease of the hypophysis is less commonly met with in acquired syphilis than in the inherited disease. He describes a case in a man aged 53 years, which, in the absence of tumour, haemorrhage, or arteriosclerosis, he considers to be one of atrophy of the hypophysis, presenting the clinical picture of cachexia following total extirpation. The general symptoms noted were the pale yellowish complexion, juvenile appearance, hairless face, and atrophy of the genital organs. Examination of the throat revealed salmon-coloured cicatrices, apparently syphilitic in nature, which suggested that the condition might be due to syphilitic disease of one of the glands of internal secretion. A history of syphilis in 1889 was obtained. During the last two years the patient had noticed weakness in the arms and legs, and loss of hair over the whole body. Latterly, he had suffered from thirst, dryness in the mouth, sexual impotence, dryness of the skin, and loss of weight. Both the Wassermann reaction and X-ray examination of the sella turcica were negative. The specific gravity of the urine was 1006. Feit draws attention to the affection of the various glandular organs, the sweat glands, testicles, and kidneys. The patient improved in general condition and gained in weight after treatment with silver-salvarsan and sulphoxylate injections.

Syphilitic and tuberculous arthritis. Roberts deplores the fact that most practitioners seem obsessed with the idea that nearly all chronic joint affections are tuberculous, in spite of Fournier's warning against this assumption more than thirty years ago.

During the last four years he has observed over two hundred cases of bone and joint disease, which, while they showed symptoms usually ascribed to tuberculosis, were undoubtedly of syphilitic origin. The behaviour of these cases under proper treatment without mechanical protection was noted, and clinical data were sought—by radiography, serum diagnosis, and other means—by which they could be differentiated from tuberculosis. It was found, however, that little help was given either by radiography or by the Wassermann reaction. The radiographs showed no characteristic points of differentiation, and the Wassermann reaction was frequently negative in the face of other evidence of syphilis and response to antisyphilitic treatment, especially in late inherited syphilis.

The similarity between the clinical pictures of the two diseases is illustrated by the fact that 51 cases of this series were diagnosed as tuberculosis by 26 experienced surgeons and treated as such for prolonged periods. In most of these a suggestive family history or signs of inherited syphilis were found. In some of them the Wassermann reaction was strongly positive, and in all of them there was a subsidence of active symptoms soon after treatment with mercury and potassium iodide. Occasionally the beneficial effect of this treatment came to a standstill, and such cases were regarded as tuberculosis developing as a subject with inherited syphilis.

The duration of the disease before treatment did not preclude the possibility of good results. Two cases of arthritis of the knee, of six and ten years' duration, recovered practically normal function. A case of spondylitis gained 16 pounds in ten weeks, and several discharging sinuses healed completely. A case of arthritis of the hip-joint of twenty-five years' standing improved in ten days. All these cases had been under continuous treatment for tuberculosis.

An instructive feature was the frequency of relapses when treatment was omitted, and the rapidity with which improvement again occurred when this was repeated. This shows the advisability of continuing treatment for a year after all symptoms have subsided. In addition to antisyphilitic treatment, where weight-bearing joints are involved, some form of apparatus should be used to protect the joint from pressure. For this purpose splints which can be removed at night and crutches are the most suitable. The local treatment of the syphilitic joint differs fundamentally from that of the tuberculous joint, where ankylosis is usually the object to be attained. Hence, any form of apparatus, such as plaster casts, for immobilizing the limb is contraindicated in the case of syphilis, except in cases of spondylitis, which should be immobilized till the radiograph shows complete repair. Roberts concludes that it is unwise to make a diagnosis of joint tuberculosis until the possible presence of inherited syphilis has been eliminated by five or six weeks' antisyphilitic treatment.

The **surgical aspects of syphilis** are touched upon by Couls, who blames most surgeons for not realizing the bearing of syphilitic infection on their problems of diagnosis and operative treatment. Surgical syphilis, he points out, concerns not only syphilitic lesions which require operative interference, but also those cases where symptoms due to syphilis simulate surgical conditions requiring operation. As examples of the latter type of case, he cites the following: cervical adenitis due to gummatous infiltration, which may be mistaken for tuberculous adenitis or for Hodgkin's disease; syphilitic mediastinitis, sometimes mistaken for malignant disease; syphilitic synovitis or bursitis, mistaken for benign conditions; syphilitic phlebitis underlying varicose veins and varicose ulcers; delayed or non-union of fractures, due to syphilitic affection of the bones; gummatous orchitis, not infrequently operated on for sarcoma or tuberculosis; joint affections due to tabes; gastric ulcer, 10 per cent. of which he considers to be of syphilitic origin, and may simulate malignant disease; the gastric crises of tabes, which have been operated on for supposed appendicitis or gall-stones. Lastly, in many injuries convalescence may be retarded by the lack of treatment of previous syphilitic disease.

For two years Schmidt has systematically examined all his (81) cases of disease of the *accessory sinuses of the nose* for syphilis. In 14 cases, or 17·3 per cent. of the total, not only was Wassermann's reaction positive, but the result of specific treatment was rapidly effective. Several of his cases gave no history and showed no clinical evidence pathognomonic of syphilis, so their syphilitic origin might well have been overlooked had not Wassermann's reaction been employed as a matter of routine.

Diagnosis. The *value of the Wassermann reaction in the control of treatment in syphilis* is discussed from different points of view by Sargent and Oettinger. Sargent first of all points out that the chief cause of error in the interpretation of this reaction is lack of appreciation of the fact that it does not detect an element in the blood which is a direct product of the spirochaete, but only an element which is commonly present in the blood of syphilitics and rarely present in non-syphilitics. This substance is probably a by-product resulting from the conflict between the spirochaetes and the defensive system of the host. This explains the negative reaction in the early days after infection, before the defensive mechanism has been mobilized. According to Sargent, it explains the occurrence of a negative reaction in the rare cases of rapidly fatal malignant syphilis and in syphilitics who are very ill or moribund, owing to the want of bodily resistance to offer combat to the spirochaetes; also the occurrence of a negative reaction in untreated syphilitics whose resistance has been sufficient to suppress the disease, and in those who have had sufficient treatment to suppress their infection either temporarily or permanently.

Sargent does not agree with the dictum that 'a negative Wassermann means nothing', but holds that when properly interpreted it may mean a good deal, both as regards diagnosis and control of treatment. The fact that the reaction frequently varies from negative to positive and inversely from month to month in cases of apparently latent syphilis must always be borne in mind. Hence the necessity for repeated examinations, and for examination of the spinal fluid, which may remain positive for some time after the blood has become negative. Sargent concludes that the Wassermann reaction is valuable as a control of the treatment of syphilis, but only when taken in conjunction with the clinical signs and the previous history and treatment of the patient.

Oettinger places less value on the Wassermann reaction as a control in treatment, while recognizing importance in diagnosis. With regard to the dictum to treat syphilis till the reaction becomes permanently negative, he remarks that in tertiary syphilis the reaction may remain positive in spite of prolonged treatment; that a reaction after becoming negative may again become positive; that an obstinate positive reaction after prolonged treatment may later on become negative without further treatment; that a negative reaction may remain negative or become positive after treatment; finally, that a patient with no symptoms of syphilis may suffer from the dire effects of vigorous treatment instituted solely on the basis of a positive reaction. As the factors concerned in these varying conditions are unknown, would it not be more scientific, he asks, and also more in the interests of the patient, to depend upon the clinical aspects of the case for the control of treatment than depend upon laboratory findings which are subject to unknown variations and frequently at variance with the clinical symptoms?

Treatment. In an instructive, if somewhat iconoclastic, lecture on some principles seldom recognized in the treatment of syphilis and the syphilitic, Graves deplores the modern tendency to neglect the *syphilitic* in the treatment of syphilis. As he remarks, many of us are acquiring the habit of disregarding the syphilitic as an individual prior to, during, and after treatment, and of treating the positive Wassermann reaction rather than the individual. The syphilitic is taught to believe himself cured when the

Wassermann reaction is negative, and is thus imbued with a false sense of security from further manifestations. Graves then poses the following questions:

(1) 'Have we any justification for the present-day teachings and practices in the treatment of syphilis?'

(2) 'Are our brilliant so-called cures now, or have they ever been, with but few exceptions, other than symptomatic cures?'

(3) 'Have we any biological or clinical evidence justifying the conclusion that the favourable influence of remedies in human syphilis is dependent upon any other factor than their influence on the defensive mechanisms inherent in the syphilitic?'

Clinical experience, he remarks, teaches us that hardly any organ or tissue may remain exempt throughout the so-called latent periods of the disease; that active symptoms may occur and recur at any period, however thoroughly the patient has been treated in the early stages; that some syphilitics are potentially or possibly inherently paretic or tabetic; that many apparently healthy syphilitics, however thoroughly treated, show positive Wassermann reactions, and most of them definite physical signs some time after so-called specific treatment, and that we have no definite means of knowing when the individual is free from infection; that clinical evidence tends to show that the virus, so long as it is present in the body, seldom, if ever, becomes wholly dormant, or latent, and that, therefore, the term 'relative tolerance' for the virus is to be preferred to 'latent'.

Graves holds that the recurrence of symptoms during the assumed periods of relative tolerance is due to many factors, among which the principal one appears to be the inherent resistance of the tissues of the individual, his habits, and environment. If the inherent resistance is defective the disease may pass beyond our control; the other factors may be more or less controlled and the resistance thereby improved, but our control of all these factors is seldom absolute and the general resistance of a syphilitic remains, as a rule, lowered.

Laboratory aids to diagnosis, in Graves's opinion, place both the physician and the patient in insecure positions, especially with regard to sanction for marriage. Personal studies of the after-history of the apparently healthy children of syphilitics, he thinks, will cause many to doubt their ability to cure the disease by any known combination of drugs, to have less confidence in present-day teachings in the treatment of syphilis, to recognize that most cures are symptomatic only, to be less willing to give sanction for marriage, and to appreciate that syphilis is a 'germ-plasm poison'. The offspring of syphilitics, he says, should be examined by comparative clinical and anthropometric methods. When such methods are applied to syphilitic families it is rare to find a child which comes up to the normal standard of healthy human breeding. Such studies will show the relative infrequency of the usual signs of congenital syphilis, but will show in many cases deviating characteristics in total development and adaptability to environment, even in the progeny of parents whom we believe to have been adequately treated.

With regard to treatment, Graves remarks that not more than 10 per cent. of syphilitics receive what can be called adequate treatment, also that active symptoms may occur irrespective of the manner or the length of treatment; therefore, that it is impossible to say when a syphilitic is cured, and also when he is no longer capable of conveying the disease to wife and children. Serological studies agree with clinical experience in showing that a relatively large number of supposed adequately treated individuals are still syphilitics, and that some of their wives and children are also infected.

Again, although clinical experience shows the beneficial result of our remedies on syphilitic manifestations, it also shows that harm may be done by over-treatment. The medicinal treatment of syphilis is still largely empirical; salvarsan, mercury, iodides, &c., are remedies, not cures. When these drugs act beneficially they appear to act by stimulating the defensive mechanism, not as direct spirochaeticides. On the other hand, they may do harm by weakening the defensive mechanism. Hence, in Graves's opinion, drugs supply only one of the conditions in the treatment of syphilis, and that not the most important. The natural history of treated and untreated cases shows that the human subject, although he has no natural immunity to syphilis, possesses considerable inherent resistance to the virus. Hence, the two fundamental principles in treatment are: first, an accurate survey of the individual's inherent resistance by a study of his family history, reaction to environment and physical condition; second, the strengthening of the inherent resistance by every possible means throughout life. Both these principles seem to be neglected when the Wassermann reaction is used as an essential indication for and a guide to treatment, when we base our treatment on so-called specifics, and ignore the teachings of clinical experience in the natural history of syphilis. A syphilitic should be subject to medical observation and study for the remainder of his life. If it is objected that such a course would lead to syphilophobia, Graves retorts that we carry out these principles in the case of other diseases, such as tuberculosis, diabetes, chronic nephritis, &c.

While in no way denying the brilliant results of our so-called specifics in the relief of the manifestations of syphilis, Graves warns us against interpreting these results as other than symptomatic cures, and advises us to regard our remedies as stimulations of the defensive mechanism rather than spirochaeticides. While aiding the defensive mechanism by means of drugs, let us not forget this mechanism is the syphilitic's most valuable asset in his struggle with his infection. With this principle to guide us, 'we shall find more to do for the syphilitic than in trying to convert his positive Wassermann reaction into a negative one; we shall then think more about the individual and less about his disease; more about strengthening his inherent resistance to, or increasing his tolerance for, his infection, and to this end we shall find many ways in addition to the use of remedies.'

For the last two years Sicard has treated cases of cerebrospinal syphilis by **small daily doses of arsenical compounds**, given either intravenously or subcutaneously. Remarkable results are said to have been obtained by this method in chronic cases of hemiplegia, paraplegia, tabes, and even general paralysis. In addition to its action on the syphilitic process in general, he states that arsenic, administered in this manner, is capable of provoking reactions of the peripheral nervous system by which spasmodic organic affections may be benefited.

When given subcutaneously the dose should not exceed 0·15 grm. dissolved in 1 c.c of distilled water. The injections are made into the adipose tissue over the fascia of the gluteal muscles, and, according to Sicard, can be given daily, with little pain and no local accidents, up to a total of 60 injections.

The arsenical preparations used were novarsenobenzol, sanar, and galyl; the two first being used without the addition of mercurial treatment.

The total amount given in cases of general paralysis during a year was 28 to 30 grm., divided into 3 courses of 3 months (9 to 10 grm.), given in daily intravenous doses of 0·15 grm.; in tabes in evolution, from 20 to 25 grm. annually, divided into 6 to 8 grm. for three months, two subcutaneous doses of 0·15 grm., and one intravenous of 0·30 grm. weekly; in spastic paraplegia, the same dose annually, but in order to obtain marked improvement in the contractures in spastic cases daily intravenous injections of 0·15 grm. up to a total of 8 to 10 grm. should be given.

Sicard states that during two years some of his patients have received 40 to 50 grm. by this method, without mercurial or iodide treatment, with greater improvement than was obtained by any other method.

With regard to side-effects, none of the severe reactions, such as 'nitritoid crises' or 'serous apoplexy', occurred in over 200 patients, treated in the above way.

Sicard suggests that the absence of these congestive or vasomotor reactions, assuming them to be caused by anaphylactic shock, may be explained by repeated small doses at short intervals neutralizing the period of anaphylactic incubation and thus insuring tolerance.

The reactions which occurred were: (1) erythema; (2) loss of tendo Achillis reflex; (3) icterus; (4) transient azotaemia. Two forms of erythema must be distinguished; the first appearing early in the course of treatment and disappearing spontaneously; the second appearing towards the end of the course and indicating arsenical impregnation and the limit of tolerance. The latter form of erythema is an indication for suspension of treatment; otherwise it may lead to severe dermatitis; even to loss of hair, onychia, plantar and palmar keratodermia, purpura, ulceration of the skin and mucous membranes, with a tendency to haemorrhage. This severe form of erythema only occurred in 2 or 3 per cent. of Sicard's cases.

Loss of the tendo Achillis reflex occurred in the majority of the cases, but loss of the knee-jerk was extremely rare, and there was only one case of general polyneuritis. The loss of tendo Achillis reflex persists long after treatment is suspended. According to Sicard, this special property of arsenic in abolishing this reflex, with the minimum of sensory and motor disturbance, may be utilized in the treatment of spastic conditions and contractures, especially those of syphilitic origin. By this means spastic paraplegic phenomena are attenuated. This improvement is attributable not only to the specific action of the arsenic on the syphilitic lesions, but also to the sedative process of this special reaction.

Icterus was only observed in 4 out of 200 cases, and was attributed to the toxic action of arsenic. It was generally benign.

Transitory azotaemia was often noted after 7 or 8 grm. of the drug had been administered. It subsided with suspension of treatment. No visual or auditory changes were found.

Sicard concludes that arsenical treatment by small and frequent doses seems to be the most efficacious and the best tolerated method. By this means the patient is submitted to intensive arsenical treatment without the danger of severe vasomotor, renal, or hepatic reactions. By means of small doses the effect of anaphylaxis is avoided, and tolerance is produced progressively. The results, as regards chronic cerebrospinal syphilis, appear to be superior to those obtained by the same quantity of arsenic administered by weekly injections, and the Wassermann reaction in the blood and cerebrospinal fluid is more easily influenced.

The daily administration of arsenical compounds is also recommended by Minet, who gives them *subcutaneously* into the tissues of the thigh, not intramuscularly. His experience with this method is limited to the later manifestations of syphilis, including gummata, aortitis, tabes, and general paralysis. The drug used was novarsenobenzol, but other preparations of the same type may be used. It is given in small doses, from 0·05 up to 0·15 grm., in series of 15 to 20 injections, the number of the series varying according to the case. At the same time, mercurial treatment is administered by daily injections of the benzoate or biniodide. Lastly, iodide of potassium is given during the intervals (10 to 15 days) between the series of arsenical and mercurial injections, up to 4 grm. daily. The results of this treatment, in Minet's experience, surpass those of any other method which he has tried. Intravenous injections he reserves for urgent cases where rapid action is required, and these also he gives daily, usually in rather smaller doses. The subcutaneous method avoids the unpleasant reactions which often follow intravenous injections. The only reaction noted by Minet was local erythema (in two cases, generalized), which disappears after interruption of treatment for a few days. An erythema appearing late in the course of treatment, however, is a sign of arsenical intolerance.

The following **modification of arsenical treatment** is advocated by Ormsby. Three injections of arsphenamine with only one-day intervals, the first dose being 0·2, the others 0·4, or in some cases 0·5 grm. This is followed by a month's mercurial treatment by inunction or injections. The three arsenical injections are repeated six weeks after the first course. This is the treatment for primary syphilis. In secondary syphilis, the first year's treatment consists of three arsenical courses as above, with 12 weekly injections of mercury salicylate (or inunction) after the second and third courses; the second year's treatment consisting of two such courses if the Wassermann reaction is negative, three courses if it is positive.

In 160 cases treated by Ormsby in the above manner, 60 remained clinically cured and had a negative reaction for periods of 1 to 3 years; 22 for periods of 6 to 9 months; 52 cases were lost sight of; and 12 were failures. These cases were chiefly late and latent syphilis, but a few primary cases remained negative for over two years.

This method gave good results in cases resistant to other forms of treatment, and there were no untoward results. Ormsby is not in favour of the method by small and frequent doses of arsenic.

Lassueur gives a favourable report on **disodoluargol,** an improved form of luargol. The latter proved to have a powerful antisyphilitic action, but presents certain difficulties in administration. It is insoluble in water, and the amount of caustic soda necessary to add in order to avoid the dangers of insufficient alkalization is badly tolerated by the veins. According to Danysz this hypo-alkalization produces a precipitation of the drug in the blood plasma, and is the cause of the vasomotor phenomena known as anaphylactoid or nitritoid crises which sometimes follow the intravenous injection of arsenical compounds.

The new preparation, disodoluargol, is free from this disadvantage and is soluble in water, forming a brown solution which remains unchanged for several hours. The proportions of its constitutents are: arsenic 18 per cent., bromine 10 per cent., silver 13 per cent., antimony about 2 per cent. It therefore contains less arsenic than neosalvarsan (20 per cent.) and much less than salvarsan (33 per cent.). Lassueur remarks that the activity of these preparations does not appear to depend on the amount of arsenic they contain, but on the affinity of their elements and the nature of their grouping.

The therapeutic action of disodoluargol, according to Lassueur, is equal to that of '606', and is obtained with smaller doses, 0·10 grm. having the same effect as 0·30 of salvarsan and 0·45 of neosalvarsan. Hence the presence of silver, antimony, and bromine would appear to play a part in this action. Disodoluargol is supplied in doses of 0·05, 0·10, 0·15, 0·20, 0·25, and 0·30 grm. Injections are made every two or three days up to a total of 1·50 or 1·75 grm. In many cases the initial dose may be 0·15 grm. The precautions and contra-indications are the same as for salvarsan and neosalvarsan, but of 100 injections given by Lassueur, the reactions were practically nil, and some patients who were intolerant of neosalvarsan tolerated disodoluargol without trouble. The effect on the Wassermann reaction was equal to that of '606'. Lassueur concludes that disodoluargol is full of promise, and a valuable addition to the therapeutics of syphilis.

Bering, from an experience of 3,200 intravenous injections of **silver-salvarsan** in 259 cases, concludes that this preparation has a rapid effect in all stages of syphilis. The doses given were from 0·1 to 0·25 grm. In his series of cases, icterus occurred 9 times and angioneurotic symptoms 6 times; there were no instances of severe dermatitis, but one case died, with punctiform haemorrhages in the brain. Bering considers that the toxic effects are less liable to occur if the initial dose is a small one (0·1 grm). The effect on the Wassermann reaction, according to this observer, is much greater when the drug is combined with mercury.

Fabry reports on a new preparation called **sulphoxylate salvarsan.** This is supplied in liquid form in ampoules, in doses of 2 to 3 c.c. It is said to be free from irritative effects and nearly painless when given by intramuscular injection. Its effect on primary and secondary lesions is said to be equal to that of neosalvarsan, and its action to be more prolonged, so that it is useful in the after-treatment of cases in which a positive Wassermann reaction persists. Fabry considers that it is best to begin treatment with a course of neosalvarsan or silver-salvarsan and continue with a course of sulphoxylate salvarsan, consisting of 6 to 8 injections at intervals of 7 to 10 days.

Stühmer is also in favour of sulphoxylate salvarsan for the after-treatment of syphilis, but remarks that further experience with this preparation is necessary before forming an opinion of its results. With regard to silver-salvarsan, he thinks an abortive cure may be obtained with this preparation in primary syphilis with a negative reaction without mercury, but in secondary syphilis combined treatment with mercury is advisable.

Dobriansky, Sequeira, and Thompson have published a preliminary note on the treatment of intractable cases of syphilis with **Query's serum.** This serum is said to be prepared by inoculation of monkeys with filtered cultures of the micro-organisms of syphilis grown on bouillon. When the Wassermann reaction in the monkey is strongly positive the serum is collected. Three cases were treated: (1) gummatous ulceration of the leg, which commenced to form healthy granulations after 20 subcutaneous injections; deafness, which was also present, also improved considerably; (2) a case of advanced tabes, with ataxia, which was improved after 20 subcutaneous and 5 intrathecal injections; (3) a case of tabes, with lightning pains, the latter being improved after 7 subcutaneous injections of the serum. All these cases had failed to respond to the usual treatment by salvarsan and mercury.

The **reactions following intravenous injections of salvarsan and neosalvarsan** have been investigated by Schamberg and Kolmer. These observers regard the theory advanced by Danysz—that the reactions are due to precipitation of the arsenical compounds after injection—as only true in part. It applies to acid and neutral solutions of salvarsan, but not to hyper-alkaline solutions (sodium salvarsan), and there is no evidence that neosalvarsan is ever precipitated in the blood. The mechanism of precipitation, suggested by Danysz, viz. conversion of the sodium salt of the drug into the insoluble base by the interaction of the sodium salt with the carbonates and phosphates of the blood, is not supported by experimental evidence. They find that both acid and alkaline solutions of salvarsan are haemolytic for defibrinated blood, while neosalvarsan is only haemolytic in very dilute or very concentrated solutions, a fact which throws some light on the relative tolerance of these drugs. Another point which they consider of importance is the difference in hydrogen-ion concentration of these two compounds; that of neosalvarsan being approximately that of blood (7), while that of acid salvarsan is lower (4·7), and alkaline salvarsan higher (9). The solution of these drugs must be perfectly clear, as a turbid solution will cause 'nitritoid crises', with syncope and shock. These symptoms, however, sometimes follow injections of a clear solution, a fact which can only be explained by the presence of an unknown impurity in certain brands of the drug.

Icterus and exfoliative dermatitis following the administration of arsenical compounds. Strathy, Smith, and Hannah have collected 58 cases in which one or both of the above conditions occurred. Out of the 58 cases, 47 exhibited jaundice or atrophy of the liver, 8 of these being fatal. Dermatitis occurred in 8 cases, 5 of which were exfoliative. Peripheral neuritis occurred in 2 cases. Albuminuria was present in more than half the cases. The onset of symptoms was seldom earlier than five weeks after cessation of arsenical treatment. A noteworthy point is the occurrence of atrophy of the liver and dermatitis in a case of psoriasis treated with Fowler's solution, in doses of 5 minims. It is also stated that these complications occurred both in syphilitic and non-syphilitic cases. For these reasons, the authors conclude that these cases of severe icterus and dermatitis are due to delayed arsenical poisoning. Their occurrence in the case treated only with Fowler's solution points to the arsenic rather than the benzol group in the salvarsan compounds as the responsible factor in such cases. They are also of opinion that the simultaneous administration of mercury may act as a predisposing cause by its action on the kidneys delaying the excretion of arsenic.

The arsenical compounds used in most of this series were neokharsivan, galyl, and novarsenobillon; but the authors are of opinion that the responsibility for these unfortunate complications lies with faulty administration and not with the drug, and that they are due to injudicious dosage and neglect of careful observation and precautions.

Ffrench, after ten years' experience with arsenical preparations in the treatment of syphilis, concludes that severe exfoliative dermatitis and toxic jaundice are rare. While working in France he had 20 cases of severe exfoliative dermatitis under his care, and concludes that the majority were due to exposure to cold. Both mild and severe cases of dermatitis may develop at varying periods during treatment, sometimes after the course of arsenical injections is completed. The prognosis is favourable when appropriate treatment is carried out as soon as the condition is diagnosed, except when lung complications develop; this occurred in three of his cases with a fatal termination.

The best form of general treatment for this condition was found to be intramuscular injection of **intramine,** introduced by McDonagh. This was given in doses of 2·5 c.c. every fifth day till the erythema in simple cases or the exfoliation in severe cases had subsided. In mild cases two doses were sufficient, but in severe cases from five to ten are often required. The action of intramine is said to be that of a reducing reagent, and its beneficial effect is explained on the theory that the dermatitis is caused by over-oxidation of the tissues by arsenic. Some cases of general erythema with high temperature were aborted by bleeding to 10 or 15 ounces, and this is recommended in all acute cases. Local treatment consisted in the usual emollient applications for moist dermatitis, and ichthyol ointment for pustular eruptions, but the length of treatment is said to have been reduced to a quarter of the usual time by the use of intramine.

Ffrench considers that there are two types of jaundice in early syphilis; one which often appears before arsenical treatment, and is syphilitic in nature and due to the toxic action of *S. pallida* on the liver cells; the second, which develops towards the end of a course of arsenical injections, he attributes to the toxic action of arsenic on syphilitic degeneration of the liver. He had fifteen cases of this type, two of which were fatal. In both the fatal cases greenish areas were found in the liver; one was a typical congenital syphilitic who developed primary syphilis. In the treatment of these cases of jaundice Ffrench found that **intramine** was also the best remedy, although in one of the fatal cases it failed. In mild cases doses of 3 c.c. are sufficient, in the severe cases ten may be required. It is given intramuscularly at intervals of five days.

The aetiology of icterus, following treatment by salvarsan and neosalvarsan, is also discussed by Nicaud, from an experience of 24 cases, 8 of which were early and 16 late icterus. Early icterus appeared during the first or subsequent courses of injections; in one case after the first injection. Late icterus appeared at variable dates, from two weeks to several months, after completion of arsenical treatment. The dose after which the condition developed varied considerably, and appeared to follow the use of certain series of preparations. The date of infection appeared to have no bearing on the development. Early icterus was generally preceded by gastro-intestinal symptoms. One case of early icterus (occurring in a subject with a previous history of malaria and dysentery) was very severe, and complicated by profuse cutaneous and mucous haemorrhages, haematuria, delirium, and irregular temperature. In two other cases there was severe diphtheroid stomatitis. Nicaud's cases of late icterus were remarkable for the absence of severe symptoms.

Nicaud mentions Milian's cases of late icterus which were improved by arsenical and mercurial treatment, but in two of his own cases this treatment, both arsenical and mercurial, aggravated the jaundice. In these cases, however, there were no concomitant signs of syphilis, while in Milian's cases these were present. The lesions found at autopsies, both in early and late icterus, have nearly all been those of acute or subacute yellow atrophy of the liver with steatosis, identical with those of arsenical intoxication. In a patient who died from cerebral haemorrhage after a third injection of salvarsan, Nicaud found diffuse fatty degeneration of the liver and round-celled infiltration round the hepatic and portal veins. Nicaud concludes that arsenic is the essential cause of the icterus, although antecedent disease of the liver may predispose to it, especially in the severe cases. Late icterus may be explained by the effect of accumulation and renal insufficiency. It is therefore important to test the renal excretion during arsenical treatment.

The **treatment of the toxic reactions** which may occur after intravenous injection of '914' forms the subject of an article by Parnell, based on a large experience of intensive treatment by '914' (40,000 injections), during which practically every form of toxic reaction occurred, but no fatalities. An analysis of these toxic effects has already been published (see *Medical Science*, 1920, **2**, 530). The present article deals with the treatment of these conditions.

The reactions may be divided into two classes: (1) immediate, which occur within twelve hours after the injection; (2) delayed, which occur after an interval of several days. Many symptoms, however, are common to both classes. The immediate reactions are seldom dangerous, but the delayed reactions are frequently so.

The **immediate reactions** are of two types: one characterized by pyrexia and cutaneous manifestations, the other by vasomotor disturbances. The treatment of the first type consists in purgation and diaphoresis, and the administration of 15 minims of adrenalin solution (1 in 1,000) immediately before the next injection, the latter being given after an increased interval. As the intervals between the injections in Parnell's cases were only two days, this interval is increased to five days, and the usual dose of 0·45 grm. is reduced to 0·3 grm. for the next two injections. In the event of a second toxic reaction following the reduced dose given with adrenalin, or the subsequent reduced dose given without adrenalin, further treatment with '914' is suspended for a month. Two toxic reactions, however slight, are, in Parnell's opinion, a contra-indication to further immediate injections.

For the treatment of vasomotor phenomena, which give rise to oedema of the face and mucous membrane of the mouth, and are usually manifested by a fit of coughing a few minutes after the injection, the immediate injection of 20 or 30 minins of adrenalin solution is regarded as a specific. It is also advised that this should be repeated at each subsequent dose.

The most important manifestations of **delayed reactions** are exfoliative dermatitis, cerebral toxaemia, and jaundice. Exfoliative dermatitis may follow a general erythema occurring as an immediate reaction, or may occur after completion of the course. The treatment advised includes opening all bullae and dressing with eusol dressings and ichthyol ointment; sulphur or ichthyol internally.

Cerebral toxaemia ('haemorrhagic encephalitis') is uncommon but often fatal. The symptoms begin with headache and vomiting, followed by epileptiform convulsions. The treatment recommended includes: injection of adrenalin (20 to 30 minims); administration of oxygen; intravenous injection of urotropin and caffein; venesection; lumbar puncture; bromides and sedatives; purgatives; washing out the stomach with magnesium sulphate and leaving sodium bicarbonate in it.

The injections of urotropin and caffein cause extreme diuresis. The bicarbonate of sodium is given on the assumption that there is an acidosis or increased concentration of hydrogen ions as in shock. Venesection relieves cyanosis, and lumbar puncture the intracranial pressure. Oxygen has been found successful when the other means failed. As the cause of the cerebral toxaemia is obscure, all the above methods should be tried.

Jaundice is an absolute indication for suspension of treatment, which should not be resumed till the skin and urine have been clear for a month. It will be noted that, although Parnell regards sulphur as useful in cases of exfoliative dermatitis, he makes no mention of intramine, which was found beneficial in these cases, and also in toxic jaundice, by Ffrench and McDonagh (see above).

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C. F. M.
C. L.

SPIROCHAETOSIS ICTERO-HAEMORRHAGICA

Epidemiology. Sobernheim, of Berne, draws attention to the following epidemiological and clinical differences between the Japanese spirochaetosis ictero-haemorrhagica and Weil's disease. The former occurs principally in rice plantations and mines; its course is decidedly more malignant, its mortality being 30–40 per cent.; the haemorrhagic symptoms are much more pronounced, and there is no splenic enlargement, which is frequent in Weil's disease. The differences, therefore, are at least as great as between the Japanese spirochaetosis ictero-haemorrhagica and another febrile disease accompanied by jaundice also occurring in Japan and known as 'seven-day fever'. These two diseases are aetiologically distinct, being caused by two different spirochaetes. On the other hand, the identity of the Japanese and German spirochaete, the possibility of which was first indicated by Noguchi, has recently been established by Kaneko and Morihana in the Berne Institute for investigation of infectious diseases. There is therefore no doubt that Weil's disease is aetiologically identical with the Japanese spirochaetosis ictero-haemorrhagica.

Although comparatively few cases of spirochaetosis ictero-haemorrhagica have been reported since the conclusion of hostilities, Garnier and Reilly maintain that cases of acute primary jaundice, which are really examples of this disease, are far from exceptional, even in peace time. The frequency of the disease during the war is attributed by them to the prolonged stay of the troops in the trenches, which were swarming with rats. Villaret, Bénard, and Dumont also report a case to show that the disease has not disappeared with the war, but is still occurring, especially in Paris, where rats are numerous, and Menetrier and Durand record two cases which occurred in Paris in March 1920.

Valassopoulo reports a case which occurred at Alexandria in October 1919, in a man aged 35, the diagnosis being confirmed by Pettit at the Institut Pasteur in Paris.

Aetiology. Spada investigated 20 rats which had been caught in the neighbourhood of the Italian Hospital, Buenos Ayres, from September to November, but in none of the animals in which sections of the spleen, liver, kidneys, and suprarenals were examined was the *Spirochaeta ictero-haemorrhagiae* found. Spada, however, does not regard these results as final, as it has been shown that while rats collected in one part of a town harbour the spirochaete, the organism is not found in the rats of another part. Thus Nicolle and Blanc did not find the spirochaete in 119 rats collected from the streets of Tunis, but found it in rats caught in the slaughter-houses of the town, and Lheritier, in Algiers, found 6 per cent. of the rats in the suburbs infected and only 3 per cent. of the rats in the port. The season is also of importance. Lheritier found 3 per cent. of the rats infected in the spring and 6 per cent. in the winter, and Nicolle and Lebailly, in Tunis, did not find any infected rats in the winter, but found the spirochaete in rats caught in the autumn. The fact that the *Spirochaeta ictero-haemorrhagiae* has been found in other parts of South America, e. g. by McDowell, in Rio de Janeiro; by Carina, at San Pablo; and Ribeyro, at Lima, suggests that further investigations will show it to be present in Buenos Ayres.

Uhlenhuth and Zuelzer examined 89 wild rats caught in different districts of Berlin, and found the *Spirochaeta ictero-haemorrhagiae*, which was pathogenic to mice and guinea-pigs, in the kidneys or urine of 9 cases. They think that the percentage of carriers is probably greater, as spirochaetes easily escape detection. The disease in rats usually appears to be latent, as the animals in question did not present any symptoms during life, and in only two cases did they show any pathological changes after death, viz. haemorrhages in the lungs.

Symptomatology. Garnier and Reilly report a case in a man aged 19, who developed a scarlatiniform rash in the stage preceding the appearance of the jaundice. The patient was sent to an isolation hospital as a case of scarlet fever, but this diagnosis was excluded by the absence of sore throat and subsequent desquamation. The diagnosis of spirochaetosis ictero-haemorrhagica was confirmed by the presence of the spirochaete in the urine, which was pathogenic to guinea-pigs. Garnier and Reilly suggest that some of the recorded cases of jaundice in scarlet fever are really examples of spirochaetosis ictero-haemorrhagica with a scarlatiniform eruption.

Lortat-Jacob and Deglaire record a case in a young man which was remarkable for the presence of intense pruritus, a bradycardia of 50–60, and colourless faeces, symptoms which are generally regarded as very rare in this disease. The diagnosis was established by the presence of the spirochaete in the urine and Pettit's serum test. Commenting on this case Valassopoulo disputes the assertion that the three symptoms mentioned are uncommon, as he has frequently observed them to be present.

The case described by Villaret, Bénard, and Dumont was an example of a transitional type between the icteric and non-icteric form of spirochaetosis ictero-haemorrhagica. Although the urine contained a large quantity of spirochaetes and the serum test was positive, inoculation of animals, which was performed on two occasions, proved negative. The writers conclude that there is not a close parallelism between the different laboratory tests, but maintain that they should always be performed systematically whenever the existence of spirochaetosis ictero-haemorrhagica is suspected.

Menetrier and Durand, who state that mild cases of spirochaetosis ictero-haemorrhagica may hardly differ at all from ordinary infective jaundice, attach some diagnostic importance to the frequency of slight haemorrhages, especially epistaxis, the intensity of the muscular pain—which is sometimes severe enough to simulate meningitis—normal coloration of the stools, and a fall of temperature when the jaundice is most pronounced.

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J. D. R.

TUMOURS OF THE BLADDER AMONG WORKERS IN ANILIN FACTORIES

The production of new growths in the urinary bladder of those engaged in the manufacture of anilin dyes and allied organic chemical materials possesses an interest extending beyond the mere question of an occupational disease. Definite chemical poisons produce in certain persons, assumed to be predisposed to it, a disease identical in its characteristics with the disease which appears in persons who have not been exposed to such poisons. The disease starts in the neighbourhood of the ureteral orifices. It is at first and for a long time latent, so that it may only become apparent long after the man has ceased to work in the factory. It gives rise to nodules, papillomas, and villous tumours, which in course of time become malignant. The malignant disease supervenes in comparatively young men. The disease can now be recognized in its early stages by means of the cystoscope, and systematic examinations with the cystoscope offer the means of recognizing in time that a worker is predisposed to irritation of the bladder in the course of his employment.

In 1895 Rehn reported 3 cases among men employed in the manufacture of fuchsin. In 1912 Leuenberger, of Basel, collected 59 cases divided as follows:

Papilloma and Fibroma	15
Carcinoma	28
Sarcoma	2
Carcinoma and Sarcoma	1
Carcinoma of the Kidney	3
Unstated	10

14 cases were operated upon, 6 of whom were living, 4 being cases of papillomas and 2 of carcinomas living one year and one and a half years respectively after operation.

Lewin in 1913 collected 33 cases occurring among those engaged in making anilin, toluidin, and naphthylamin, the last a by-product in the making of naphthol, which in itself is a harmless substance.

In a case noted by Lewin the man had ceased to work in anilin for 6 years, but, during the time he had been working, 12 of his fellows had suffered. Lewin found that he had a carcinoma which had already become inoperable.

Nassauer collected 32 cases from his own observation in the course of 19 years and concluded that anilin was the cause, combined with an individual predisposition.

Of the cases of tumour of the bladder in the Frankfurt University Klinik between 1895 and 1918, 25-30 per cent. were due to anilin.

Oppenheimer, of Frankfurt-a.-M., met with 20 cases between 1910 and

1919 in men between 34 and 47 years—an age not generally subject to bladder growths. During 12 years at a factory employing on an average 68 men there had been 15 middle-aged men affected, and some of them had died of the disease. In another factory employing about 60 men there had been 27 bladder cases, of whom 9 had died. In a third factory employing about 30 men, in the course of 10 years 29 had died of new growths in the bladder. As the growths take years to develop, many cases, from one cause or another, are lost to the enumeration, so that such statistics as the above are not exhaustive.

Among the materials connected with anilin to which the workers are exposed are benzidin, naphthylamin, toluidin, and creasol compounds. It is not only the actual contact with the materials, but exposure to fumes, e.g. on the part of members of the clerical staff, which is productive of the disease. Nassauer cited 8 such cases in the Frankfurt Hospital.

It is remarkable that in these cases of bladder disease there was no simultaneous trouble induced, either in the respiratory or the alimentary tract, or indeed in the kidneys, including the pelvis of the organ. Apparently the urine remaining for a time in contact with the epithelium of the bladder sets up an irritation which it has not time to produce in the pelvis of the kidney.

Of the 20 cases noted by Oppenheimer, 12 were already malignant, but the earlier cases presented papillomas and soft villous growths; in one case the papilloma had persisted for 7 years without becoming malignant. The men had been working for periods between 2 and 28 years, an average of 18 years, before they came under observation. In two cases the men had ceased the occupation for 10 and for 17 years respectively, before the onset of symptoms. The latter had worked for 2 years, and then 17 years after ceasing the work he presented a villous growth the size of a berry. Of course the inference that the growth was due to the anilin irritation can only be supported by collecting similar instances. There is, indeed, a period of latency not marked by any local or general signs, yet which may possibly be revealed by cystoscopic examination.

In a man working with benzidin there was observed by cystoscopic examination the growth of a carcinoma projecting to the size of a cherry in the course of three months. Papillomas have been seen with the cystoscope six weeks after an exploration of the bladder by suprapubic cystotomy, when there was no sign of them. No relation between the length of the exposure, or the concentration of the fumes, and the production of a new growth in the bladder has been observed, nor any relation between the production of a papilloma and a carcinoma. A papilloma has developed 12–15 years after the commencement of the exposure: a carcimona developed in one case 2 years, and in another 4 years, after the commencement of the work. Six men worked together under precisely the same conditions; after 20 years 2 remained quite well, 2 had new growths of the bladder but had recovered after treatment and remained quite well, 2 were dead of new growths of the bladder.

In 1916 a man aged 42 had a first attack of haematuria after working for 26 years in a part of a factory in which others had suffered from tumours of the bladder.

He presented 3 papillomas, 1 at the right and 2 at the left ureteral orifice, which were removed at several sittings by means of the cold snare and by electrolysis. He remained free until the middle of 1918; in April

1919 there was a nodular tumour the size of a walnut in the bladder-wall near the left ureteral orifice which felt hard per rectum. A carcinoma had developed on the base of one of the papillomas, whilst the site of the papilloma on the right side remained sound.

Papillomas are especially localized about the ureteral orifices, but this was found not to be so generally the case with carcinomas.

In 18 of the 20 cases the results were known as follows: 9 had died of the growths, in 1 death was expected, 1 had died of intercurrent disease, in 2 carcinomatous cases the result of treatment and the ultimate termination remained in doubt. There remained 5 cases of papillomas which had been relieved by treatment. Oppenheimer concluded that the prognosis in the case of carcinoma was unfavourable, in the case of papilloma the result was always in doubt.

The treatment adopted was that of removal of the papilloma by the cold snare followed by electro-coagulation by diathermy. If this failed a suprapubic incision was made, the tumour destroyed by diathermy to avoid inoculation, followed by excision. Exposure to X-rays afforded no benefit whatever.

5 cases were treated by suprapubic cystotomy and excision.
- 1 of papilloma died 1 year after, of intercurrent disease, without recurrence.
- 1 of carcinoma recurred after 6 months, and he died 1 year after the operation.
- 1 of carcinoma was free from recurrence after 3 years.
- 1 of carcinoma, after excision of half the bladder and the end of the ureter, was free from recurrence 4 months after the operation.
- 1 of carcinoma, rendered anaemic by bleeding for 2 years, died after total extirpation of the bladder and diversion of the ureters to the loins.

6 cases were treated by intravesical methods:
- 1 case was free from recurrence after 18 months.
- 1 case was free from recurrence for 2½ years, and then developed carcinoma.
- 1 case suffered from reappearance of papillomas at different spots.

Recent cases of malignant disease have all been described as carcinomas, none of sarcoma.

Among the measures proposed for prevention are good ventilation, masks containing sponges, rubber gloves, clothes to protect the skin, daily baths, work under dangerous conditions to be restricted to half-yearly periods, alternating with half a year out of danger.

A systematic control by cystoscopic examination should be applied to all men who exhibit any bladder irritation and the exclusion from further exposure of men who have exhibited any sign of bladder new growth.

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W. G. S.

DIAPHRAGMATIC HERNIA

Increased attention has been directed to the subject of diaphragmatic hernia owing to the occurrence of a number of cases during the war. Men were struck by bullets which passed through the chest in a more or less longitudinal direction from the point of entry. The left chest was penetrated in a tangential manner without the injury being fatal. The men were hit whilst lying prone, or, whilst upright, by shrapnel balls or by bullets from aeroplanes aloft.

An allusion was made to tangential injuries of the thorax calling for immediate interference in the *Medical Supplement*, 1918, **1**. 201. But cases which at first appeared to need merely expectant treatment manifested later the peculiar characteristics of diaphragmatic hernia which were noted by the early authorities. Paré, who first described this injury, noted that the man apparently recovered after a wound penetrating the chest, but later suffered from a weak stomach and colic; finally, after suffering acute abdominal pain, he died, eight months after the injury.

Most of the colon had prolapsed through a wound in the muscular part of the diaphragm, the opening not being larger than the tip of the little finger. The prolapsed part of the colon had become greatly distended. Sennert reported that a young man in attempting to commit suicide ran his sword through the left side of his chest from the 4th rib in front to the 9th rib behind. The wound healed in two months, but seven months after the injury he was seized with severe vomiting, the vomit became black, and he died. The sword had made a circular opening in the tendinous portion of the diaphragm, through which the whole stomach had passed into the chest, the lung had become completely collapsed, the heart pushed over to the right side. The stomach was gangrenous and the gangrene had spread to the omentum and pancreas. These observations controvert the statement in the Aphorisms of Hippocrates, which include injuries of the diaphragm among those necessarily fatal. Morgagni added other conditions besides, viz. that seen in infants from congenital causes; also the so-called true hernia through the oesophageal opening giving rise to acute strangulation.

The case quoted by Astley Cooper occurred in a woman and ended in acute strangulation at the age of 28; when younger she had occasional attacks of epigastric pain, difficulty of breathing, cough, and vomiting, then vomiting became more frequent, with pain and no movement of the bowels for some days before death. There was found a circular opening, 2 inches in diameter, in the centre of the left half of the diaphragm through which the transverse colon and omentum had prolapsed and become gangrenous.

The case clearly demonstrated that, like external hernias, diaphragmatic hernia is a progressive lesion, which, at first latent, then troublesome, suddenly develops an acute phase and is rapidly fatal. Peacock's case illustrated the production of the hernia by a crush between buffers, in other instances between a waggon and a gate-post, or by a fall of earth. Peacock's case was a man aged 50, who some time before had been crushed between buffers, yet had recovered and had followed his work as a porter until attacked by typhus fever, of which he died after 11 days. The impairment of resonance found in his left chest was taken to indicate pneumonia, which indeed existed on the right side. But there were no recent lesions except those resulting from the typhus fever. Yet through a gap in the left tendon of the diaphragm, large enough to admit the hand, a portion of the abdominal viscera had prolapsed, including, the stomach, the spleen enlarged and softened by the fever, the large intestine from the caecum to the sigmoid flexure, and nearly the whole of the small intestines.

Hill in 1870 described a typical case of the so-called true hernia through the oesophageal opening, at the same time that it presented the confusing sign of oesophageal obstruction and the absence of vomiting owing to a kinking at the junction between the oesophagus and stomach. A coachman aged 50 had always enjoyed good health until a year before, when there ensued a gradually increasing difficulty in swallowing which reduced him to a skeleton and he was starved to death. The stomach and omentum were absent from the abdomen, the upper end of the duodenum was traced up to a ring in the right half of the diaphragm. At about 1½ inches from its termination the oesophagus was sharply bent on itself, and it turned upwards to the right into the stomach, which occupied a hernial sac in the right pleura. The wall of the hernial sac was formed by the parietal peritoneum as an inner layer and the parietal pleura as an outer one.

In a very similar case described by Hale and Goodhart death occurred by exhaustion produced by vomiting. A man aged 49 begun to suffer from acid eructations and occasional vomiting; the vomiting became more frequent and he died of exhaustion. In a hernial pouch between the two crura of the diaphragm there was an orifice extending from the oesophageal opening on the left to the opening for the vena cava on the right. Into the sac had passed the pyloric end of the stomach, the pancreas, duodenum, and transverse colon. This case was diagnosed as cancer of the stomach, Hill's case as cancer of the oesophagus; in the latter the prolapse of the fundus of the stomach had kinked the oesophagus and prevented vomiting; in Hale and Goodhart's case the prolapse of the pylorus made vomiting the cardinal sign.

The surgical treatment of diaphragmatic hernia was first undertaken for indications deduced from the obvious injury. Postempski in 1889, having previously observed a case in which a stab had ended 4 months later with fatal strangulation, when he met with a second case, operated without delay. A boy aged 14 presented a stab wound in the 11th left intercostal space, 2 cm. in length, in the post-axillary line. Through this the omentum had prolapsed for 5–6 cm. The wound was enlarged, the 11th and 12th ribs forced apart, the prolapsed omentum excised, a wound in the diaphragm, 1·5 cm. in length, sutured, clots in the pleural cavity removed, and the wound in the chest wall closed without drainage. There was temporary surgical emphysema and pneumothorax, which subsided spontaneously, and the patient was exhibited 3 weeks later quite recovered, except for some signs of pleural thickening.

Knaggs in 1904 referred to previously published cases and included one of congenital hernia through the oesophageal opening, which became strangulated, in a woman at the age of 29. The case was too late for the operation to be completed.

When the diaphragm has been ruptured by crushing of the chest wall, although an immediate operation is indicated, yet the condition of the patients is unfavourable. An operation for closure was attempted in two cases of buffer accidents by Roughton and by Berry, and although unsuccessful, yet an attempt to close the rent offered the only chance.

Keith in 1910 gave a full account of congenital defects in the diaphragm, with embryological explanations, and he enumerated 34 specimens in London museums, with a description of the position of the defects.

The three cases operated upon by W. J. Mayo, as described by Beckman, unfortunately exhibited excessively large defects in the diaphragm.

Case I. A male aged 17, weighing 110 lb., had had increasing gastric trouble from an early age, which had latterly only been partially relieved by gastric lavage. An exploratory operation discovered the absence of the left half of the diaphragm. A hugely dilated stomach filled the abdomen, from which the duodenum passed into the left thorax, which contained all the intestines down to the sigmoid flexure. No further operative procedure was attempted.

Case II. A man aged 47 had had for the past 7 months distress after food, followed by vomiting in 15–30 minutes; with this occurred attacks of diarrhoea. The patient refused operation for a supposed ulcer of the stomach, but a year later, as the vomiting had increased in frequency, he returned. He had then a right irreducible inguinal hernia which was first operated upon. At a second operation, the stomach was found prolapsed through a very wide opening in the diaphragm to the left of the aorta. The stomach was withdrawn and sutured into the opening in the diaphragm, the chief object being to prevent its distension in the thorax. The patient made a good recovery and remained well when last seen.

Case III. A woman aged 47 had increasing frequency of vomiting after food and lost 100 lb. in weight in the course of 3 years. On abdominal exploration, an opening in the diaphragm in the position of the oesophageal opening was found, through which the whole stomach had prolapsed and had become adherent to the hernial sac. The adhesions were as far as possible separated and the stomach stitched into the opening. There was an uneventful recovery.

A number of cases of diaphragmatic hernia due to gunshot injuries have been recently reported in English, French, German, and American publications, all illustrating the peculiar features of the injury. After expectant treatment in hospital and repeated medical examinations, there was a return to active or restricted duty, then a slowly increasing, obscure disturbance, in some cases finally diagnosed by an X-ray examination; in other cases the acute phase supervened, quickly followed by death. It has been clearly demonstrated that the only measure by which a diagnosis can be made is by X-ray examination. But that examination demands special experience, for the condition has been frequently overlooked in such examinations.

Diaphragmatic hernias have remained unsuspected until discovered in the course of a routine X-ray examination of the chest. Thus Howk and Hering examined a man who complained of a tickling cough, loss of weight and strength, indigestion, and constipation. A left diaphragmatic hernia was discovered; then, on further questioning, the patient stated that 20 years before, at the age of 13, he had been struck on the abdomen and rendered unconscious for a quarter of an hour. For some years there was no trouble, then headache and migraine occurred every 3 or 4 days with nausea, relieved by bilious vomiting.

Belden noted a similar instance in a man who had been wounded in many places, including the left chest. After healing he complained of weakness, heartburn, and vomiting, 1–1½ hours after meals. On his return to New York from France he was pale, emaciated, had heartburn, pains in the epigastrium, and he vomited a portion after every meal. Nothing was made out until the chest was examined by the X-rays when a left-sided diaphragmatic hernia was discovered, part of the stomach having prolapsed into the thorax.

The mode in which rapid death may ensue in the case of diaphragmatic hernia is shown by Guleke, the patient dying from pressure, not only on the left lung, but also, through the mediastina, upon the opposite lung, the heart, and the venae cavae. A soldier was wounded in the left chest by shrapnel which set up haemoptysis. After he had lain out for 15 hours he was brought to the Field Hospital severely cyanosed, in great dyspnoea, with a pulse-rate of 140. The left thorax was not moving, the right moving excessively; there was a tympanitic note up to the left 2nd rib, with no breath sounds, and above that breathing as of a compressed lung. The bullet had entered 3 fingers' breadth internal to the left nipple-line, at the level of the 2nd rib, and had made exit at the lower margin of the ribs in the axillary line. The patient died before any operation could be undertaken. It was subsequently found that the diaphragm had been split in the course of its fibres to the length of 8 cm., starting from its junction with the pericardium. This had been caused by the bullet striking the diaphragm almost at a tangent. The stomach, from the oesophagus to the pylorus, had prolapsed into the thorax and had become so greatly distended as to push the heart, lungs, and mediastina well over to the right. Whilst increasing frequency of vomiting has been one of the chief symptoms, it may be absent owing to a kink at the lower end of the oesophagus, as in Hill's case mentioned above, also in one of Obendörfer's cases.

A soldier had been wounded by a fragment of shell from an aircraft, one year before. After a time in hospital he had returned to service and was at work in a field bakery, when he was suddenly seized and died in a few hours without vomiting. The abdominal cavity was found normal except that the stomach was fixed in the diaphragm. Its fundus had passed through, the left lung was completely collapsed. The prolapsed stomach had apparently undergone post-mortem digestion and had ruptured. There was a hole in the diaphragm the size of the palm of the hand, circular, with callous margins, to which the stomach had become adherent. In a mass of scar tissue surrounded by a little pus was found a fragment of shell. The end of the oesophagus and the commencement of the duodenum were both closed by kinking.

The recognition that diaphragmatic hernia is a progressive lesion, and the desirability of operating as soon as the condition is discovered, is confirmed by the case described by Symonds. The man was wounded in February 1916 by a bullet which entered through the left scapula and lodged under the skin of the left hypochondrium, from which it was removed.

He vomited blood, but the wound healed and he returned to duty. An attack of abdominal pain occurred for the first time 6 weeks after the injury; it recurred three or four times a month; it arose after a meal, was increased in severity by constipation, and vomiting of food did not give relief. The condition was discovered on X-ray examination seven months after the injury, and expectant treatment with rest in bed pursued for 14 days more. Then, following an acute attack of pain, the patient collapsed into a desperate condition. An abdominal exploration had just discovered a hole in the diaphragm, when the patient died. There was found *post mortem* a circular opening in the left half of the diaphragm which admitted a medium-sized hand, through which the stomach, transverse colon, omentum, and upper portion of the small intestines had passed. The stomach reached up to the second rib; all the viscera were of a plum colour and kinked; the apex of the heart was just to the left of the sternum.

The paper by Els from Garré's Klinik in Bonn contains a good summary of the subject and emphasizes two important points, the desirability of an X-ray examination by means of the screen with the patient standing upright, and the advantage of thoracotomy and the separation of the ribs as the general operative procedure, the abdominal incision being only suitable for simple cases without adhesions.

Cases have long been treated for seropneumothorax, for pleural effusion with thickening of the parietal pleura or for haemothorax. In the absence of a careful X-ray examination a patient has been treated for vague gastric or chest trouble. The symptoms have been misleading—pain and constriction in the lower part of the chest and epigastrium, as if the heart and lungs were compressed, with palpitation and dyspnoea. There may be dysphagia, also vomiting after taking anything more than a very small quantity of food. Relief from the desire to vomit may be found by lying down on the left side when that is the side of the hernia, whereas lying on the right side then aggravates the tendency. Presumably the latter increases and the former diminishes the kink in the stomach, passing through a gap in the back part of the left side of the diaphragm.

For examination the patient should be standing before the X-ray screen, when the line of the diaphragm on the left side may be noted as horizontal, but waving with the least movement. Above this line is an air-space, its upper margin dome-shaped, and above this the left lung denser than the right lung because compressed. The heart is displaced to the right behind the sternum. In order to distinguish this appearance from that of a pneumothorax, an oesophageal tube is passed, the descent of which may be followed without filling it with opaque material. The end of the tube may be noted to curl up into the air-space; if gas then escapes, the air-space will be diminished; if air is blown down the tube, the air-space will be increased. Also the air-space will vary in extent at the different examinations. As the patient swallows material containing barium or bismuth, a check may be noted at the lower end of the oesophagus, with a temporary dilatation of the gullet above. Then some of the opaque material flows into the stomach above the diaphragm and fills part of the air-space. This is favoured by the patient lying down with the pelvis raised. As the meal passes through the pylorus into the duodenum it may be noted that the duodenum has been displaced to the left. If it be the colon which is engaged in the hernia, then the course of the meal has to be observed until it reaches the splenic flexure. The actual opening in the diaphragm cannot be generally seen, but may be indicated by an hour-glass constriction in the opaque material filling the stomach.

Relaxation of the diaphragm on one side follows upon a permanent lesion to the corresponding phrenic nerve whether by injury or by disease. It is called by some eventratio diaphragmatica, but this term should be avoided, for eventratio is strictly speaking more applicable to prolapse of the abdominal organs through a gap in the diaphragm, and as a matter of fact has been employed in that sense by Guleke. Relaxation of the diaphragm may be distinguished from diaphragmatic hernia when the patient is observed by the X-ray screen whilst standing. The diaphragm moves with respiration, only to a less degree than on the sound side. On holding the breath and contracting the abdominal muscles, the relaxed half makes an abnormal ascent. On filling the stomach and intestines with opaque material the organs can be recognized as lying below the level of the diaphragm. Moreover, the symptoms are relatively slight of compression, consolidation, or atelectasis of the lung of that side.

An epigastric incision is indicated as an exploratory measure in doubtful cases, and in uncomplicated cases, when there is a small non-adherent hernia through an opening at the back of the diaphragm, it may be possible to reduce the hernia and close the opening. But under the most favourable conditions there is nevertheless the negative pressure in the thorax and the positive pressure in the abdominal cavity to contend with.

When adhesions have occurred it becomes impossible to withdraw the prolapsed stomach, colon, omentum, or pancreas; there is a danger of tearing the organ and the negative pressure in the thorax becomes a great obstacle. Indeed, attempts at reduction have had to be abandoned; or the omentum can be divided between ligatures, leaving the distal part in the thorax. In all except the simplest cases it is best to make a long intercostal incision between the 6th and 7th ribs, which are then widely separated, giving access to the pleura. Adhesions between the stomach or colon and the pericardium can now be separated. The gas can be squeezed out from the distended gut, or failing that may be aspirated. Then the hernia can be reduced without the necessity of enlarging the opening in the diaphragm. Further, the collapsed lung can be freed, drawn forward, and sutured so as to favour expansion. After sewing up the opening in the diaphragm from above, the chest wound should be completely closed. Any subsequent collections of fluid may be aspirated; even if reaccumulations of fluid turn to pus, the resulting empyema will be only limited in character and yield to further surgical treatment.

In Andrew's case a bullet entered the left chest behind, 2½ inches from the middle line, below the 12th rib, and lodged 2 inches below and 1 inch internal to the left nipple-line, under the skin, whence it was removed the next day. This occurred on March 12, 1917. After healing and a period of convalescence, the man returned to his depot and was sent to France on July 27. He had begun to complain of pain after food and occasional vomiting, but was ordered medicine and duty. The vomiting recurred more frequently until he became very weak and he was sent home on December 28 with the diagnosis of gastritis. After another year in hospital, and again periods of convalescence and home duty with medicine, he was discharged on July 25, 1918, with the diagnosis of gastritis. After various steps on the part of the Pensions Committee, he was at last submitted to a thorough X-ray examination, on February 19, 1919, when ¾ of the stomach were noted to be in the left thorax, reaching up to the 3rd rib. Following upon this, on March 25, 1919, laparotomy was done, the stomach withdrawn, the adherent omentum divided so as to leave the prolapsed part in the pleural cavity, the gap in the diaphragm closed, and a good recovery followed. In the similar case operated upon by A. J. Evans, the lesion had been overlooked for 11 months. The entire stomach and omentum were found in the left pleural cavity. A similar operation and result followed.

In Barton's case the condition was overlooked for 20 months. A sergeant was wounded by a bullet from an automatic pistol on April 15, 1917; the bullet entered over the left 8th rib close to its junction with its cartilage, and made exit in the left loin 2 inches from the spine. The wound healed after a time at home, and he was returned to France in September 1917. Then the vomiting which had previously been occasional recurred every evening after marching, but was considered a triviality. By October 1918 his condition had become so bad that he was sent back to England. Finally a severe attack of pain and vomiting with constipation led up to the operation on December 14. The epigastrium was first opened and the hernia recognized, but it was impossible to withdraw the stomach, so portions of the 7th and 8th ribs were excised, the gas squeezed out of the stomach, and it and the omentum reduced, through the rent in the diaphragm, which was quite 2 inches in length. The left lung had undergone total collapse. After closing the diaphragm, also the chest and abdominal walls, there was a good recovery, although slow, delayed by the gradual expansion of the lung.

A more prolonged case still, under Greig, involving both an abdominal operation and subsequently an extensive resection of the chest wall was set up by a bullet wound on October 23, 1914, and recovery dated only from January 1919.

A striking case, exhibiting the necessity for a thoroughgoing X-ray examination, was described by Soresi. An American soldier aged 20 was wounded by a fragment of shell which entered to the left of the xiphoid cartilage. He was unconscious for 30 hours; he vomited blood, and blood escaped from the wound, and this continued for some days; later there was occasional vomiting after food. There were several X-ray examinations until after 5 months, when signs of a fragment of shell in the upper part of the left abdomen and of pleural adhesions above the diaphragm were noted. This led, 8 months after the injury, to an abdominal exploration for the removal of the fragment, about the size of a grain of maize, which was found behind the lesser curvature of the stomach. But, presumably because attention was solely directed to this object, nothing more was noticed. Subsequently repeated vomiting reduced the man to a skeleton and gastro-jejunostomy was suggested. But upon an improved X-ray examination a hernia through the diaphragm of a portion of the stomach was discovered. Thereupon the stomach was reduced, the opening in the diaphragm closed, and after recovery the man returned to military duty.

In Harttung's case, operative treatment came too late. The man was wounded in January 1917 by a shrapnel ball which entered the left shoulder and was removed from under the skin of the left groin. He was 3 months in hospital suffering from pain in the left chest and abdomen, especially on breathing, with haemoptysis. He was afterwards on garrison duty until the end of the war. On March 14, 1919, after jumping from a wagon he was seized with acute abdominal pain and vomiting. The next day he walked to the hospital, where at first nothing definite was made out. Then on the 16th the left chest was punctured, and, brownish-red stinking fluid being drawn off, an operation for empyema was undertaken under local anaesthesia. In the course of this operation a coil of intestines was noted in the pleural cavity, but nothing more was done until the next day. Then the patient was in the stage characteristic of late abdominal obstruction. An abdominal incision was made also under local anaesthesia, but as the hernia could not be withdrawn, and the patient's condition was bad, an artificial anus was made in the transverse colon. There followed a sloughing of the prolapsed gut in the thoracic cavity, increasing septic absorption, and death on June 7. There was found in the diaphragm at the level of the 8th rib in the anterior axillary line, 3 fingers' breadth from the inner aspect of the ribs, a slit parallel with the muscular fibres 2 cm. in length, admitting a finger. Through this the splenic flexure of the colon had prolapsed and subsequently undergone gangrene and sloughing. The left lung was completely collapsed.

In a similar but rather less severe case under Seiffert a lateral anastomosis was first made between the dilated ascending and the collapsed descending colon. Then the abdominal incision was extended through the diaphragm into the thorax. Adhesions which had formed in the course of the 2nd year since the injury were separated, the transverse colon and omentum reduced, the lung freed and stitched forward, and then all closed. The only complication was two sinuses, through which the silk sutures closing the diaphragm ultimately escaped.

Els described three cases.

Case I. A soldier on September 25, 1914, was wounded by a bullet which entered the left thorax at the level of the sixth rib between the anterior and mid-axillary lines and made exit posteriorly at the level of the 12th dorsal spine, about two fingers' breadth to the left. Pain, dyspnoea, haemoptysis, and fever followed, and blood-stained fluid was aspirated. After recovery he was treated by repeated punctures for seropneumothorax with displacement of the heart. Early in 1915 he had increasing symptoms of difficulty in swallowing, frequent vomiting, shortness of breath, and loss of 30 pounds in weight until March 1916, when the chest was opened through the 7th intercostal space, the stomach, spleen, and omentum separated from their adhesions and reduced; the lung was also freed, and a slit-like opening in the diaphragm, 10 cm. in length, sutured. The chest wound was closed, and 5 days later bloody fluid aspirated; a limited empyema supervened, which necessitated a plastic operation to close a cavity the size of the fist. In June 1918 he had regained the loss of weight and was able to do full work.

Case II. The bullet entered below the left scapula, which set up haemoptysis and pain in the left side on breathing. Later there was increasing gastric disturbance with vomiting after food, relieved by lying down on the left side. There was loss of flesh. On X-ray examination, the air-space was noted to extend a hand-breadth above the diaphragm. A month after the injury a laparotomy incision was made, the stomach withdrawn, and adherent omentum divided, leaving the prolapsed portion in the pleural cavity. Three months later the lung had re-expanded, he had gained 50 pounds in weight, and had made a complete recovery.

Case III. The left shoulder was lacerated by fragments of shell on March 30, 1915. Slight haemoptysis followed, and there was very little gastric disturbance for half a year, during which treatment was directed to the wound and the resulting limitation of movement of the shoulder. He first vomited 4 weeks after the injury, but after six months it began to be frequent, 10 minutes after food, until he could only swallow a little at a time and then lie down for an interval of 10 minutes or so, on his left side. The diaphragmatic hernia was only discovered 3 years after the wounding. On opening the chest through the left 7th interspace, the stomach, colon, and omentum were found prolapsed into the pleural cavity and all much adherent. Also the lung was quite compressed. After separation and reduction with freeing of the lung, a hole in the outer part of the left quadrant, which would admit the fist, was closed. 500–800 cm. of blood-stained fluid was aspirated on three occasions within 5 days, then an empyema formed, which healed after three months from the operation. A subsequent examination showed that the lung had expanded to a great extent, but there was still a diminished respiratory movement on the left side. The orifice in the diaphragm was completely closed, and the man had put on 20 lb. weight.

Schwartz and Guénu, summing up experiences regarding left diaphragmatic hernia in France, concluded that the general procedure should be an incision along the 7th left interspace, curving downwards over the left rectus, the incision extending from the line of the axilla to the umbilicus. The rib cartilages being divided and the wound retracted, the margin of the diaphragm is divided until the hernial orifice is reached. After reduction of the hernia and the freeing of the lung, sutures are applied in stages from the diaphragm outwards and the pleura temporarily drained.

Diaphragmatic hernia is much less frequently noted on the right side, partly owing to the liver, partly to the more fatal character of the injuries on that side. Higgs met with a case on the right side in a stout woman aged 34, who, whilst carrying a washtub full of water, resting against her abdomen, felt a sickening pain followed by nausea. She then became subject to nausea, acid eructations, and vomiting, with increasing frequency for 2½ years. On X-ray examination the barium fluid was noted to pass through a constriction in the region of the pylorus, but as the level of the diaphragm was not noted, the case was diagnosed as one of pyloric obstruction. At the operation nearly the whole of the omentum and the transverse colon, together with the pyloric portion of the stomach was found to have passed through a rent in the diaphragm, to the right of the middle line, between the two lobes of the liver. The opening in the diaphragm was antero-posterior in direction, 13 inches in length, 1½ to 2 inches of the diaphragm intervening between the opening and the ribs. The aperture was closed and the patient recovered, completely relieved from her symptoms.

Frank's case was an instance of congenital diaphragmatic hernia on the right side. A boy aged 16 had had from infancy occasional attacks of vomiting which had become very frequent and severe during the previous three weeks. A right-side hernia through the diaphragm was diagnosed by means of an X-ray examination. On opening the abdomen the liver was found pushed to the right, the stomach, duodenum, a large part of the omentum, and a small part of the liver were engaged in a sac protruding into the right pleural cavity. The sac was formed by peritoneum which had herniated through an enlarged oesophageal opening. Reduction could not be completed owing to the negative pressure in the chest. At a second operation, 17 days after the first, the chest was opened by excising 5 inches of the 7th rib; even then reduction was difficult owing to the positive pressure in the abdomen. The sac was not removed but included in the sutures closing the opening in the diaphragm. Recovery followed, and an X-ray examination showed the stomach in its normal position.

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W. G. S.

OBSTRUCTION OF THE PORTAL VEIN AND ITS TRIBUTARIES

An addendum to the review of 'Ascites and its Surgical Treatment', see *Medical Science*, 1920, **2**, 244, is furnished by the post-mortem examination of cases of portal-vein obstruction described by Kaspar, in Vienna. There are many sources, the clinical signs are obscure, the diagnosis often impossible, and a post-mortem examination is the sole means of discovering why the surgical treatment has failed to arrest the progress of the ascites.

Case I. A man aged 54 had been a heavy drinker. Syphilis was denied, and the Wassermann test yielded a negative result. In the summer of 1918 he began to complain of pain in the region of the liver, with slight swelling of the abdomen. Diarrhoea followed, some of the stools being coloured black. He lost flesh, became pale, had oedema of the ankles and sacrum, the heart was found enlarged to the left; the liver did not project more than a finger's breadth below the ribs; the spleen was only slightly enlarged. There was free peritoneal fluid which reaccumulated after it had been removed twice by paracentesis. Hence, in March 1919, a hardened calf's artery was inserted into the right lower quadrant of the abdominal wall. An oedematous swelling occurred which extended to the scrotum, the tapping had to be repeated, diarrhoea, with melaena, continued, and he died in July 1919. There was found *post mortem* cancer of the body and tail of the pancreas, which had compressed the portal vein and caused chronic obstruction and a persistence of the ascites. The liver had undergone atrophy without cirrhosis and the spleen was only slightly enlarged. The intestinal coils and mesentery were oedematous, also the oesophageal veins were dilated. The inner end of the calf's artery, projecting into the peritoneal cavity, was entirely buried among coils of intestine adherent to the parietal peritoneum.

Case II. A man aged 60 had had from childhood a small umbilical hernia. After the age of 22 he had gradually developed a bilateral enlargement of the thyroid gland due to multiple adenomas, but which did not cause trouble. At the age of 38 he acquired a left inguinal hernia, which, when he was 52, became strangulated, and for which an operation was done. At the age of 53 he had an attack of haematemesis and melaena for which he was a week in hospital, but subsequently had no gastro-intestinal disturbance. He wasted during the war, the left inguinal hernia recurred, followed by a similar hernia on the right side. As this hernia became painful, he entered hospital on January 11, 1919. Then a moderate degree of ascites was discovered and also the existence of irreducible herniae in both inguinal regions and at the umbilicus, but nothing more abnormal was then noted. Alcoholism and venereal disease were denied. The right inguinal hernia was operated upon, during which 500–600 c.cm. of clear yellow fluid escaped from the peritoneum; at the same time the umbilical hernia was treated. There followed a rapid reaccumulation of peritoneal fluid with slight oedema of both lower extremities. On February 2 there was severe haematemesis and melaena which persisted until death on February 6. There was found old-standing chronic ulceration of the pyloric third of the stomach with a recent erosion into the gastro-duodenal artery. Around the end of the stomach and the commencement of the duodenum were a mass of old adhesions from which the common bile-duct and the hepatic artery were dissected out, free from all compression. But the portal vein had undergone obliteration from the head of the pancreas up to the portal fissure. This had occurred by thrombosis and a thrombus extended into the splenic and superior mesenteric veins, which was of more recent formation. As a result of this obstruction there had occurred a marked dilatation of gastric and duodenal veins in the gastro-hepatic omentum and of the commencement of phrenic vein, constituting a cavernous condition, partly thrombosed, partly communicating with the branches of the portal vein within the hilum of the liver. The liver was somewhat atrophied, but not cirrhotic; the spleen was enlarged by interstitial fibrosis. There was a considerable collection of clear dark yellow fluid in the peritoneum.

Case III. A woman aged 39 suffered for a year from pain in the back and epigastrium, with a feeling of fullness in the stomach. Eleven days before death pain spread to the left flank; two days before death she was seized with acute abdominal pain and vomiting, tympanites and severe melaena. The diagnosis before death was perforation of a duodenal ulcer with peritonitis. There was found thrombosis of the portal and superior mesenteric veins, with consecutive infarction of the whole of the jejunum and part of the ileum, with sero-fibrino-haemorrhagic peritonitis. A small duodenal ulcer had penetrated the back wall and set up periduodenitis and the infarction, which had extended into the spleen and up into the liver. The thrombosis of the portal vein was of old standing towards the liver; towards the commencement of the vein it was more recent. There had resulted a dilatation of the gastric, phrenic, and oesophageal veins which had sufficed to compensate the portal vein obstruction until eleven days before death.

Case IV. A woman aged 42 had noted an increase in girth of her abdomen for a year without gastric disturbance. She was pale, wasted, and after paracentesis the spleen was felt enlarged, the liver could not be felt. The Wassermann reaction was positive. After four months of medical treatment with paracentesis, omentopexy was done in March 1919 and no further tapping was required for 2½ months. In June a hardened calf's artery was inserted. She died in July. There was found syphilitic cirrhosis of the liver, with shrinkage of the left lobe and hypertrophy of the right. The trunk of the portal vein had been obstructed by an old-standing thrombosis, and there had been a more recent thrombosis extending into the splenic and the superior mesenteric veins, along with infarction of the intestine. The thrombosis had been started by the syphilitic disease of the liver and had spread against the current. There had occurred compensatory dilatation of the gastric, phrenic, and oesophageal veins which had sufficed until the recent extension of the thrombosis into the tributaries of the portal vein.

Case V. A man aged 39, after eating a bad sausage, was seized with acute pain in the upper abdomen. The pain continued for a week, when he ceased to pass motions, and the abdomen became tympanitic, especially in the upper part, with a pulse-rate of 120. Therefore, ten days after the commencement of the illness, he was operated upon for acute intestinal obstruction, when some free peritoneal fluid escaped; the small intestines were empty, the first part of the colon distended. After the division of a band at the splenic flexure, the contents of the colon passed on into the previously empty descending colon. After the operation and an enema, a motion followed, but signs of peritonitis continued, and he died a day after the operation, on the eleventh day of the illness. There was found a recent thrombosis of the portal vein and its tributaries with haemorrhagic infarction of the upper portion of the jejunum, sero-fibrinous peritonitis, enlargement of the spleen, an enlargement of lymphatic glands in the portal fissure. The bad sausage had set up gastritis, the gastritis an enlargement of the lymphatic glands, and this enlargement compression of the portal veins and thrombosis.

Case VI. A man aged 43 had suffered two years before from rheumatic fever with endocarditis and arthritis. Afterwards he had cardiac disturbance on exertion, a feeling of weight in the epigastrium, and occasionally melaena. Three days before an acute attack of abdominal pain set in with flatulence and blackish fluid in the motions. He was operated upon on the diagnosis of perforation of a gastric or duodenal ulcer, when infarction of most of the small intestines and the mesentery was exposed. 2·5 meters of the intestine were excised, but the patient died the next day. There was found an old-standing thrombosis of the splenic vein, with recent thrombosis of the superior mesenteric vein and a commencing thrombosis of the portal vein. There was besides a recent thrombus in the abdominal aorta which extended into the coeliac axis, the splenic and superior mesenteric arteries. The spleen had become generally adherent from perisplenitis to the diaphragm and was undergoing recent necrosis. There was old-standing mitral disease. In this case the sequence of events was the rheumatic fever, endocarditis, endophlebitis of the splenic vein or splenitis, followed by the endophlebitis. The recent thrombosis constituting the terminal lesions had extended from the splenic vein. Previous to the last illness the portal vein obstruction had been compensated by the adhesions of the spleen to the diaphragm, connecting the splenic venules with the phrenic veins.

After a long review of cases previously published in Germany, Kaspar concluded that there followed upon the obstruction of the portal vein a dilatation of its tributaries, which communicated through the gastric vein with the branches of the portal vein in the hilum of the liver beyond the obstruction, also with the veins of the diaphragm and oesophagus. This produces an almost cavernous-like tissue in the gastro-hepatic omentum, which should not be taken for a cavernous new formation, nor for a congenital abnormality. The effect on the liver of portal vein obstruction is in the direction of atrophy. A chronic ulceration, such as that in the duodenum, may obstruct the portal vein either by compressing it or by originating a thrombosis. Diagnosis before exploration is difficult or impossible; an exploratory operation is important, because of the possibility of removing compression on the portal vein. In the case of thrombosis of the portal vein, an early epiplopexy is indicated before ascites has become well established. Delay until acute complications have supervened, as in the cases described, renders surgical interference of no avail, because too late.

Kaspar, F. Beiträge zur Kenntniss des Verschlusses im Pfortaderstamm und der Vena lienalis. Kavernöse Umwandlung der Vena portae und chronisches Ulcus duodeni. *Deutsche Ztschr. f. Chir.*, 1920, **156**, 1.

W. G. S.

ACIDOSIS IN ITS RELATION TO PROBLEMS OF RESPIRATION

In the years preceding the war, respiratory problems were receiving an increasing amount of attention from competent investigators. As in many other cases, research received the stimulus of the need for exact knowledge bearing upon such questions as high flying, wound shock, gas poisoning, and anaesthesia. It was early recognized that rational treatment must be based upon sound physiological knowledge. The result has been that during the last five years there has been an intensive study of the factors involved in the respiratory process, both upon the more physical and chemical features of the process, as well as upon the more physiological mechanisms concerned. The work has been fruitful in modifying many of our views and in pointing the way to better therapeutic methods.

With regard to the part played by the blood, research has tended to emphasize the complexity of the physical and chemical factors involved, among which may be mentioned the reaction of the blood, the conditions for the carriage of oxygen by haemoglobin, the carriage of CO_2, and the relative parts played by the plasma and by the corpuscles in this carriage. In the blood, these various factors seem to be welded into a complex equilibrium, such that a displacement of one or more factors tends to bring about a shift in the majority of the others. The problem is further complicated by the fact that under unusual or pathological conditions substances other than the normal may appear in the blood and exercise their influence in displacing the equilibrium. It is not unnatural to find that there is still controversy over certain of the details of the work, which is increased by the fact that it is almost impossible for a single set of observers to work at more than a few aspects of the problem at one time.

For the purposes of discussion it is convenient to divide the subject into the broad headings of:

(1) The more purely physical and chemical aspects.
(2) The physiological aspects.
(3) The more medical aspects.

(1) Physical and chemical factors. **Oxyhaemoglobin and the carriage of oxygen in the blood.** Views upon this subject have not undergone much recent change. The work of Barcroft and his associates has cleared up the salient features upon which the use of haemoglobin as a respiratory pigment in the body depends. It has been shown by them that temperature, the salts of the blood, and the reaction of the blood all play their part in turning the chemical reaction represented by the equation $Hb + O_2 = HbO_2$ into one useful to the body. Under the conditions existing in the blood oxyhaemoglobin will take up oxygen at the pressure of the lung and give it up again at the pressure of the tissues. A more acid reaction will make the oxyhaemoglobin take up slightly less oxygen in the lung, but will increase its power of giving up oxygen to the tissues. In illustration of how the knowledge concerning this aspect of the question is becoming standardized, it may be mentioned that the relation between the percentage saturation of haemoglobin with oxygen and the pressure of oxygen to which it is exposed has been found by Barcroft and A. V. Hill to be expressible within the limits of experimental accuracy in mathematical terms, to wit

$$\frac{y}{100} = \frac{kx^n}{1 + kx^n}$$

where y is the percentage saturation of the haemoglobin with oxygen and x is the pressure of oxygen to which the sample of haemoglobin is exposed, n and k are two constants of which fortunately n is nearly constant for man. We are also able now to relate mathematically the reaction of the blood to this equation. There are further equations relating the reaction of a sample of blood to the amount of bicarbonate present. In this connexion we are fortunate that so gifted a thinker as L. J. Henderson should be investigating the more mathematical side of the question. His work throws further emphasis upon the beauty of the complex physico-chemical equilibria appearing in the blood.

With regard to oxyhaemoglobin itself, the evidence seems to be clear that oxyhaemoglobin is a stronger acid than haemoglobin. Oxygenation of the blood therefore slightly increases its acidity. This was originally suggested by the work of Haldane, Douglas, Christiansen, and has been confirmed by others (Hasselbach, Parsons). The chemical meaning of the fact is very obscure, but it would seem to have the following use to the blood. When the CO_2 leaves the blood in the lung, there should be a slight change to an alkaline reaction. This is, however, compensated by the extra acidity of oxyhaemoglobin. The converse will happen in the tissue. It is a fine adjustment in the buffer system which will be discussed below.

The carriage of CO_2 by the blood. The opinions held as to the compounds by which CO_2 is carried from the tissues to the lungs fall into two main classes. First it is assumed that CO_2 is combined only as sodium bicarbonate. To this is added the view that the sodium is shared between the proteins and the CO_2. It is therefore a competition between two acids of different strengths. This view really goes back to the time of Loewy and Zuntz, but it has been expressed more forcibly lately by Haldane, Hasselbach, and Parsons, of whom the latter has analysed the matter mathematically. Recently Poulton and Campbell have also taken this view as expressing the normal conditions in the circulating blood. The second view is that the CO_2 is very largely carried in combination with the proteins of the blood, in especial with oxyhaemoglobin. This dates back at least to the time of Bohr.

It has been brought up again by Buckmaster, and quite recently by Mellanby and Thomas in a slightly modified form. In considering the controversy, one is rather reminded of the truth and limitations of the good old saying that there is nothing new under the sun, and at such a time the reviewer is naturally cautious. It would seem that there really is an element of the truth upon each side of the controversy. In the case of the proteins, of which we may take haemoglobin as an example, we are dealing with amphoteric substances. Such substances possess both acid groups and basic groups. At a certain definite reaction known as the isoelectric point (Michaelis and Takahashi) the protein will change its properties from behaving mainly as an acid to behaving as a base. Upon the acid side of the isoelectric point, being a base, the protein will combine with a substance such as CO_2, whereas upon the alkaline side of the isoelectric point the protein will act as an acid displacing CO_2. The discrepancies may therefore be cleared up to a certain extent (as Campbell and Poulton point out) by taking into consideration this property of haemoglobin. Above a certain pressure of CO_2 (pressure in excess of that in the body), haemoglobin can combine with CO_2; below that pressure, when the surrounding medium is not acid enough to shift the reaction over the isoelectric point, the protein will tend to displace CO_2. Since the pressure of CO_2 in the blood is not large enough to change the reaction of haemoglobin to the acid side of the isoelectric point, in the body normally the conditions lead to the carriage of CO_2 by bases, chiefly sodium.

In their paper, Mellanby and Thomas bring into the question an interesting new point. It has not been clear in the past why shed blood gradually lost its power of combining with CO_2 upon standing. They have shown that blood under these conditions develops lactic acid. This is produced by the corpuscles, as it does not occur in the plasma alone if the corpuscles are centrifuged off. Our conclusion at the moment would be that normally most of the CO_2 is carried by the sodium in the blood, but that under exceptional circumstances the proteins may play their part.

The buffer action of the blood. Intimately related with the question of the carriage of CO_2 is the question of buffer action. A solution containing buffer substances has the property of taking up relatively large quantities of acid without producing much change in the reaction of the solution. Blood has this power to a marked degree. If 1 c.c. of HCl be added to 100 c.c. of distilled water and to 100 c.c. of blood respectively, the acidity of the water will change much more than that of the blood. Buffer substances usually belong to the class of weak acids, of which the phosphates, bicarbonates, organic acids, are good representatives. In the blood we have bicarbonates, phosphates, and amphoteric proteins, all of which may possibly serve as buffer substances. There has been some controversy as to which substances actually are acting as buffers (B. Moore, Bayliss). It is now generally accepted that, within the limits of reaction usually found in the body, the bicarbonates and the protein together are practically entirely responsible for the buffering action.

The buffer action of the blood takes place both in the plasma and in the corpuscles. As pointed out by Hopkins, in his address, the corpuscles virtually serve as a reservoir for CO_2. With increasing pressure of CO_2 more CO_2 passes into the corpuscles (Campbell and Poulton). Coincident with this change there is a shift of the inorganic ions of the blood. With increasing CO_2 pressure, chloride and sulphate ions migrate into the corpuscles. In some way this shift is associated with an adjustment of equilibrium between the corpuscles and the plasma. By means of it more sodium is probably liberated for combination with CO_2.

Physiological Mechanisms

The stimulus to the respiratory centre. In 1905, as the result of the work of Haldane and Priestley, it was held that the stimulus to the respiratory centre was two-fold.

(1) Excess of CO_2, and (2) diminished oxygen tension, when the alveolar tension of oxygen was considerably reduced.

The experiments of Winterstein and Hasselbach, in which they injected acids into the blood-stream, demonstrated that a more acid reaction of the circulating blood *per se* would stimulate the respiratory centre. This was followed by the belief (Haldane) that the exciting mechanism was really an increased acid reaction of the blood. Some recent experiments by Scott and Yandell Henderson rather take us back to the older views. An acid reaction of the circulating blood will certainly excite the centre, but it appears that CO_2 itself may excite it. Other substances, such as morphia, which do not modify the reaction of the blood will depress its activity. The truth can probably be held to lie in considering the respiratory centre as a group of cells particularly sensitive to certain stimuli. Like all cells, an increased reaction or an increase of CO_2 tension leading to a change in the condition of the cell or a change brought on by diminished oxygen tension will all tend to modify the activity of the cell.

The reaction of the organism to low pressures of oxygen and the alkaline reserve. Views upon this subject are becoming somewhat changed. It has been a currently accepted doctrine for some time that the body reacted to diminished oxygen supply in the following way. The diminished oxygen caused the production in the tissues of the body, chiefly the muscles, of substances of an acid nature, e.g. CO_2 or lactic acid. The latter has been shown by Fletcher and Hopkins to appear in isolated amphibian mammalian muscle in the absence of the oxygen supply. The respiratory centre was stimulated by change in the reaction of the blood, whether this reaction is produced by excess of CO_2 or by other acid substances. This led to a simple explanation of the increased respiration observed upon exercise or breathing diminished tensions of oxygen. Acid substances produced in the tissues were carried to the respiratory centre, and there the blood, which was more acid in reaction than normal, stimulated the centre, resulting in an increase of breathing, and so a washing out of CO_2 from the blood. In this way the body was able to get its reaction back to the normal again, being assisted further by the kidneys. Fixed acid now took the place of carbonic acid in the blood. The result of this was that there was a diminution in the bicarbonate capacity of the blood, termed by Van Slyke the 'alkali reserve'. This excellent term has been applied rather differently by different writers. The term 'alkali reserve' was introduced by Van Slyke to express the amount of alkali which is available for the transport of CO_2 in the blood. Though its exact definition has been slightly modified by some, it seems most convenient to regard it as measured by the amount of CO_2 which is taken up by a given sample of blood or plasma at 40 mm. pressure of CO_2. This gives the idea a measurable basis. For a normal blood it is usually in the region of 50 volumes of CO_2 per hundred volumes of blood. Variations in the alkali reserve may result in:

(1) Decrease of available sodium due either to the combination of acids such as lactic acid with part of the normal CO_2-carrying sodium, or to an actual depletion of Na from the blood (as has been recently shown), or (2) increase due to the presence of increased sodium. A diminution in the alkaline reserve should then follow the effects of fixed acid circulating in the blood as the result of oxygen want. Up till recently diminution in alkaline reserve has been rather tacitly understood to mean the presence of acids other than carbonic in the blood. The body retrieved an acidotic condition by the action of the respiratory centre and the kidneys. Now in what way has the position become modified?

Though there can be really no doubt that we have to deal in most cases with a condition in which the presence of fixed acid in the blood causes changes in breathing, fresh facts have come to light which mean that we have to consider other effects as well. In the Monte Rosa expedition, apparently acid bloods were found, containing no increased lactic acid at rest. An explanation was suggested at the time for the condition (Barcroft) upon the lines that instead of there being present increased acid in the blood there was a depletion of base. More recently, J. S. Haldane, Kellas, and Kennaway found that, in the increase of breathing produced by exposure to low atmospheric pressures, the urine did not become acid but became alkaline instead. This conclusion was also reached by the American workers Yandell Henderson and Haggard. The latter found that if they made an individual breathe into a bag in which they absorbed the CO_2 with potash, there was an increase of breathing which could not be correlated with a decrease in the alkaline reserve of the blood. They have pointed out that the body tries to keep its reaction at a constant level and that it may do this in one of two ways.

The reaction of the blood is determined by the ratio $\frac{H_2CO_3}{NaHCO_3}$. Increase of the value of this ratio in the blood causes a more acid blood, and decrease the reverse. When there is a decrease of the bicarbonate of the blood by forced breathing, CO_2 tends to be washed out of the blood. The result of this is that there is an upset of the equilibrium, which may have to be adjusted either by increasing the CO_2 or acid, or instead by reducing the amount of Na present. In a condition where excess breathing is produced, we then may have the following conditions: first slight acidosis, then excessive breathing in which CO_2 becomes washed out of the blood, 'an acapnial process,' then the inability of the tissues to supply CO_2, followed by a condition in which, owing to the upset of the normal ratio $\frac{H_2CO_3}{NaHCO_3}$, the blood is more alkaline than the normal. As the maintenance of reaction is a most important one to the body, it is essential to reach a condition again in which the ratio $\frac{H_2CO_3}{NaHCO_3}$ has again the same value. This can be done either by the excretion of sodium or by the removal of it from the blood to the tissues. When the reaction has been adjusted by the removal of sodium in this way, an estimation of the alkaline reserve will show a lowered CO_2 capacity. It will be indistinguishable by the CO_2 capacity method alone from the condition in which there is sodium combined with fixed acid. In reality the condition is very different.

It has been found that forced breathing and breathing diminished tensions of oxygen both lead to the formation of alkaline urines. Further, Macleod and Knapp have found that the giving of alkalies by the mouth tends to cause excretion of lactates in the urine, presumably as a neutralizing process.

Briefly put, the new ideas crystallize down to this. According to the older conception we regarded the whole matter in terms of a shift of the equilibrium (in which the reaction plays a large part) to the acid side. We forgot that we were dealing with a balance which might be upset also by a shift of conditions to the other side of the blood reaction point. This has now been corrected. We have both a condition in which the reaction of the blood may shift to the acid side and one in which the blood may shift to the alkaline side. Both will require the calling into action of protective mechanisms on the part of the body. In the case of acidosis, the mechanism will be the respiratory centre washing out CO_2 and the excretion by the kidney of the excess of acid as soon as it can. Further, under conditions where there is an increase of acid in the blood, there is a lessened combination of ammonia and CO_2 to form urea, so that increased amounts of ammonia appear in the urine. In the case of an increase of alkali, there may be increased excretion of base, as sodium bicarbonate in the urine, an excretion of sodium lactate, or, as Davies and J. B. S. Haldane and Kennaway have shown, a diminution of ammonia excretion with an increased excretion of urea.

Given the two conditions—that is, a diminished alkali reserve due to acid and one due to the alkalosis—we may distinguish between the two, according to Yandell Henderson, upon the following lines. If we make the subject breathe air containing excess of CO_2 (7 per cent. CO_2) the acidotic subject will be harmed. The patient suffering from a blood reaction which is too alkaline will be considerably improved. Henderson claims that cases suffering from the latter condition after ether anaesthesia have been benefited in this way by the administration of CO_2.

The passage of oxygen through the lung. The controversy which has raged for so long as to the question of whether the alveolar membrane of the lung acts as a passive structure in the passage of oxygen through it, or whether it has a more vital property, seems to be settled now. Barcroft's experiment, in which he lived for six days in a glass chamber, gradually exhausting the store of oxygen during this time, is now familiar history. In this experiment it was shown that when the tension of oxygen was decreased in the alveolar air to an amount corresponding to some 18,000 feet there was no evidence that the blood was charged with oxygen at any higher pressure than the alveolar air. The subject in question had the blood taken from an artery. It was quite blue. Though Haldane still would be in favour of the possibility of a secretory process, it seems fairly clear that the amount of oxygen passing into the blood is conditioned by known laws of physics and chemistry and that no special extra factor is necessary to explain the mechanism. The matter, of course, is of consequence in connexion with the question of maintenance of high altitudes in flying.

MEDICAL ASPECTS

Acidosis. At the last meeting of the British Medical Association the question of acidosis formed the basis of a discussion. In his opening address, Prof. Hopkins raised a plea for the great need of defining this term. The discussion which followed raised a number of aspects of the problem, without, however, really defining the situation. Suggestions made at the meeting seem to offer some hope in this direction, and it is proposed to consider them here. Before putting forward the suggested scheme of classification, it is necessary to recall to the reader what has been said about the physiological mechanisms. If foreign or abnormal amounts of fixed acids are produced in the body, the buffer action of the bicarbonate and proteins together in the blood is first utilized as a protective mechanism against the dangerous condition of changed reaction of the blood. Any slight acid change in reaction stimulates the respiratory centre, resulting in an increase of breathing and a washing out of CO_2 from the blood, until the normal reaction is again reached. This leaves the blood with a lowered alkaline reserve, as measured by the CO_2 capacity method. Some of the available sodium is now combined with the fixed acid. This picture will be the most usual one to appear. In addition, certain recent research is tending to show that if, by reason of a painful wound or a diminished oxygen tension, the body is induced to breathe more violently than normal, and so wash out large amounts of CO_2 from the blood, a change in the opposite direction may set in. The protective mechanism in this latter case will be the removal of alkali from the blood by excretion or withdrawal to the tissues, until the reaction is again normal. In this case, too, a measurement of the alkaline reserve by a blood sample will show a lowered alkaline reserve due to the depletion of blood alkali. By CO_2 capacity measurements, both conditions will appear to be the same, and both will have less sodium available for the carrying of CO_2 from the tissues in a sudden muscular exertion. The subjects, however, will react differently to breathing a slight excess of CO_2. In the former case extra CO_2 will exaggerate matters, in the latter an excess of CO_2 should improve them, by gradually calling back alkali into the blood. At the moment all such cases of changed blood reaction, with sodium combined with fixed acid and depleted alkali, are classed under the heading of acidosis. The difficulty of suggesting a scheme which will cover all conditions is of course clear. The following one seems to have some merits, and it is based upon the discussion at the meeting of the British Medical Association.

Scheme.

A. *Blood reaction*	More acid than normal	*Acidaemia.*		
	More alkaline	*Alkalaemia.*		
B. *Alkali reserve*	Increased	*Alkalosis.*[1]		
	Diminished (*Acidosis*)		Alkali combined with fixed acid	*Compensated acidosis.*
			Alkali depleted	*Alkalipenia.*
C. *Acetone bodies present*	Ketosis.			

This scheme has the advantage of distinguishing between altered blood reaction and altered alkaline reserve. Both may vary independently.

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[1] The word 'Alkalosis' is here used in a rather different sense to that of some writers. It seems, however, to be the logical one.

Very often both will occur together. Though the word acidosis has some disadvantages there seems no doubt that it has come to stay.

To the clinician, it is of paramount importance to have some simple tests to apply for these different conditions, and here, at present, it is felt that the correlation of clinical experience with physiological research is badly needed. For alkaline reserve we have the estimations of CO_2 percentage in the alveolar air, and of the bicarbonate capacity of the blood; for the reaction of the blood, the indirect technique developed by Dale and Evans. It must be confessed, however, that methods of this nature cannot be applied at all generally by the average practitioner. They require expert manipulation.

Is it possible to distinguish clinically between any of these types, of which the most general will be acidaemia, compensated acidosis, and ketosis? Ketosis will have the test of acetone bodies in the urine, and will therefore be easily distinguished. A lowered alkaline reserve, measured by the CO_2 capacity of the blood, will tell us that the case is one of acidosis; this should be further indicated by a lowered alveolar CO_2 percentage. We are left with distinguishing between compensated acidosis and alkalipenia. If the kidney is normal, some indication should be obtained from the reaction of the urine. An acid urine might mean that we were dealing with a case of compensated acidosis, and an alkaline one that it was the rarer condition of alkalipenia.

For distinguishing clinically between acidaemia and alkalipenia, the only ready test would appear to be the normal respiratory centre. It is clearly proven that an increased frequency of breathing supervenes when the blood reaction becomes more acid than the normal. Acidaemia should therefore be accompanied by hyperpnoea. The condition of alkalaemia should give rise to apnoea. In using the respiratory centre as a test, it must be remembered that many other factors (nervous or otherwise) may alter its normal activity. An instance of this appears in the hyperpnoea produced as a response to breathing low tensions of oxygen. A decrease of normal irritability may also be produced by the administration of morphin, or by the failure of activity produced by excessive oxygen want. A good illustration of this latter condition was sometimes seen in gassed patients in France, where administration of oxygen to a badly gassed case produced a temporary increase of breathing (or even real hyperpnoea), the explanation being that oxygen woke up a failing centre which was then able to respond to the increased reaction of the blood and by breathing rid the body of its excess of CO_2. In concluding this part of the discussion, it is perhaps justifiable to call attention to the true significance of acidosis, in view of the ideas prevalent in some directions that acidosis is a disease itself. Really acidosis is a symptom which usually appears as the result of other abnormal conditions. In its turn, disturbance of the blood equilibrium may of course lead to various troubles. For instance, in diabetes, compensated acidosis will appear first. As the limit to which compensation can occur without changed blood reaction is reached, acidaemia will set in. There is now not enough buffer present to deal with increasing quantities of acid, and so a vicious circle may be started. The acidosis has brought in its train many troubles, but in the first instance it was initiated by the changed biochemical conditions underlying diabetes.

Shock. This is another instance of a case in which acidosis is not a cause but an effect. The Reports of the Committee upon Surgical

Shock and Allied Conditions demonstrate clearly that shock is primarily a condition of stagnation of blood in the capillary area, brought about by several factors, among which may be mentioned the absorption of toxin substances from wound surfaces. Owing to the stagnation of the blood, the tissues become inadequately supplied with oxygen, so that a condition of acidosis (with its diminished alkaline reserve) tends to appear.

Whether the condition of alkalipenia as the result of over-breathing produced by painful wounds (Yandell Henderson) may also be an attendant factor in shock, must be left to further research to decide.

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R. A. P.

ABSTRACTS

SURGERY

Nassetti, F. Fistole conseguenti a lesioni esposte delle ossa. [**Post-traumatic bone sinuses.**] *Arch. ital. di chir.*, 1920, **2**, 1.

Nassetti's account of post-traumatic osseous fistulae is based on 208 cases, which include lesions of almost all the bones of the skeleton. The article is in two sections: in the first a systematic account is given; in the second the several bones are considered in order.

Attempts have been made to cure these fistulae by means of the injection of polyvalent sera and the local application of antiseptics. Comparatively small and superficial foci may be cured by these means, but, as a general rule, a cure can be effected only by surgical measures, namely, the complete removal of the focus of infection. For the successful performance of the operation an accurate knowledge of the characters and forms of the inflammatory foci is indispensable.

Periostitis. Occasionally a simple thickening of the periosteum is found, without any appreciable evidence of osteitis, the suppuration being maintained by threads of cloth or minute fragments of metal embedded in the fibrous tissue. More frequently a chronic periostitis of this kind is associated with a cortical osteitis. Equally rare are cases of osteoplastic periostitis with absence of signs of osteitis. In these cases bony masses, sessile or pedunculated, and varying in size and form, are found adhering closely to the bone and projecting into the soft tissues. They originate probably from flaps of periosteum stripped from the bone or completely detached. On the other hand, such osteophytes are frequently met with in connexion with foci of osteitis, or at the orifices of osseous fistulae.

Osteitis and osteomyelitis. Whatever the bone affected, both rarefactive and condensing osteitis are found associated. In spongy bone the former generally predominates; the latter is well marked, and reaches the degree of eburnation, in cases which have been chronic from the first. The focus is not always situated at the original site of the injury: occasionally it appears to have arisen in a zone of indirect injury, and in some cases it is necessary to assume that a progressive diffusion of the infection has occurred.

In relation to the bone itself, the focus is cortical, central, or terminal. Cortical osteitis is almost always the result of open contusions, of grooving by tangential injuries, or of fissures either isolated or associated with other lesions. Central osteitis is frequently met with in voluminous masses of callus resulting from comminuted fractures. It also occurs without external deformity of the bone as a sequel of simple perforation. Terminal osteitis is not infrequently met with in one of the two stumps projecting into an irregular callus, in the bone-ends in pseudarthroses, and in amputation stumps.

The degree to which the original focus may have extended beyond its original limits varies greatly. All gradations are met with between a circumscribed cortical focus and long lines and surfaces of osteitis involving the greater part of the diaphysis and at times the epiphysis. Similarly with central foci, these may involve the whole length of the bone and involve the neighbouring joints. In the irregular masses of callus which form round comminuted fractures it is usual to find one or more recesses passing off in various directions; these may be of great length (10–15 cm.), often communicate with cortical foci, and in many cases evidently correspond to fissures radiating from the primary seat of fracture. Occasionally, more than one independent focus is present.

Osteomyelitic cavities are of two types: spheroidal or ovoidal, and canal-like (tunnels), the latter being complete, with two orifices, or ending blindly, in which case the blind end is usually expanded. The tunnels have well-defined bony walls of the consistence of ivory; their inner surface is usually smooth, though at times rendered irregular by osteophytes, and is covered with a layer of fungating granulation tissue, in which sequestra may be embedded. Tunnels are almost always the result of perforation by a projectile, and minute metallic particles are not uncommonly found in their walls; they are, however, at times produced by unduly prolonged drainage.

Ovoidal and spherical cavities are mostly found in the long bones, generally in the meta-epiphyseal region, and canals situated in the epiphyses tend to take this form rather than that of typical tunnels. The cavities lie either in the substance of the bone, which then shows no external deformity or sign of fracture, or in the centre of a mass of callus. Their walls are identical in structure with that of the tunnels and often contain sequestra or foreign bodies. The pus secreted by them finds exit by one or two channels, varying in length and generally corresponding to the track of the projectile.

In operating for the removal of the inflammatory focus the bone should be approached through an incision planned on the normal anatomical relations, without reference to the fistula. The latter is often in a position unfavourable for the complete exposure of the diseased bone, or endangering important vessels and nerves. If the fistula corresponds in position to the normal anatomical route the cicatrix and fibrous tissue surrounding the track should be excised, bearing in mind the possible necessity for a plastic operation in the case of extensive cicatrices. The fistula, if it does not correspond to the anatomical incision, may, as a rule, be left untouched, and will heal spontaneously when the focus which maintains it is removed. It may, however, be advantageously excised in cases where there is a probability of both wounds healing by first intention.

On reaching the bone the periosteum is incised and separated from the bone, together with the overlying soft parts, and automatic divaricators are applied so as to bring the area of diseased bone fully under observation. Areas of inflamed periosteum are then excised well into healthy bone, and osteophytes searched for and removed, a radiogram being of great service in ensuring their detection.

In circumscribed **cortical osteitis** the pitted surface should be scraped away down to healthy bone and the thickened margins carefully levelled. Levelling of the edges is of special importance in treating grooves formed by tangential wounds, since the bony deposits are apt to encroach on the groove itself. When the osteitis follows the line of a fissure this should be followed in its whole length and converted into an open groove. In this manœuvre it is important to avoid perforation of the medullary cavity and consequent infection of the medulla.

Osteomyelitic cavities should be widely opened. **Canals,** when complete, are best opened by removing the more slender of the two bridges of bone bounding them and enlarging the cavity so as to produce a broad excavation. The removal needs to be performed cautiously and piecemeal, in order to avoid fracture of the bone. In cases where the remaining bridge of bone would be insufficiently strong and late fracture liable to occur, it is preferable to make the excavation comprise one of the orifices of the canal, and in complete canals of the epiphyses Nassetti always adopts this method. The same line of treatment is adopted in the case of blind canals. It is not always desirable or necessary to make the excavation at the orifice of the canal: its position will be determined by the anatomical route chosen and the requirements of adequate drainage.

Osteomyelitic cavities generally call for extensive removal of bone. Guided by a probe inserted into the cavity, the operator first enlarges the fistula and then removes piece by piece the layer of bone covering in the cavity, the eburnation of the tissue often rendering the use of cutting forceps necessary. The fungating lining of the cavity is then scraped away, and sequestra and foreign bodies removed. This stage in the process needs to be carried out with great exactness, so that every part of the wall may be thoroughly exposed and not a trace of rarefactive osteitis left. When healthy bone is reached the sharp spoon is said to emit a characteristic sound ('cri de l'os sain'); if this is not obtained, careful examination should be made to discover a possible recess or patch of fibrous tissue. Finally, the vertical margins of the excavation are smoothly levelled down. A difficulty arises when a track runs deeply and opens on the surface at a distance from the excavation made. To open up such a track completely by removal of one of its sides would, in most cases, render the remaining bone unduly weak. In these circumstances, Nassetti approaches the recess of the cavity by a second incision, thus creating two excavations in the bone, with ample communication between them.

For drainage Nassetti uses simple aseptic gauze. This is applied in the form of folded pieces placed side by side and vertical to the raw surface of the bone. The ends are cut off level with the surface of the external wound, and care is taken that the angles of the latter are held well open by the gauze. Complete closure of the wound can be performed in certain cases only, where, for instance, the osteectomy has been carried out through an anatomical incision situated at a distance from the fistula.

The dressing is changed on the sixth or seventh day, provided no complications have arisen. At this and subsequent dressings the gauze is applied more loosely, though still reaching to the depth of the wound; and after the third or fourth change, if the discharge is not abundant, the granulations appear healthy, and there is no retention of discharges, the drain is discontinued. Over-prolonged drainage will itself maintain suppuration and may lead to the formation of a fistula.

When the inflammatory process involves an entire segment of the bone (diaphysis, epiphysis) resection has necessarily to be resorted to.

T. W. P. L.

Ferrarini, G. Sulla terapia delle fistole del dotto di Stenone ed in particolare sull' operazione di disinnervazione della parotide proposta dal Leriche. [**Parotid fistulae.**] *Arch. ital. di chir.*, 1920, **2**, 207.

Many cases of parotid fistula, especially the premasseteric variety, are readily cured by establishing a new intra-oral excretory opening, and at times the ultimate re-establishment of the normal passage occurs. On the other hand, the treatment of old masseteric and retromasseteric fistulae, associated with obliteration of the distal portion of the duct and the presence of cicatricial tissue in the deeper structures, presents great difficulties. As evidence of this Ferrarini refers to no less than twenty-six different methods as having been suggested for their cure. These methods, a discussion of the relative values of which forms the main subject of Ferrarini's paper, may be classified as follows: (1) the re-establishment of the normal passage; (2) the replacement of an external by an internal or intra-oral fistula; (3) the re-implantation of the duct; (4) the plastic reconstruction of the duct; (5) the suppression of the parotid secretion; and (6) the creation of a collateral passage through the submaxillary gland.

The first of these methods, whether carried out by means of progressive dilatation by sounds inserted through the mouth, or by suture of the severed duct, directly or combined with the formation of a flap of oral mucosa, is obviously available only in cases where the distal portion of the duct has remained pervious. It is adapted more especially for the treatment of wounds of recent date, in which the separation of the divided ends of the duct is not extensive.

The second method, effected by puncture of the cheek through the external fistula, followed by prolonged drainage of the intra-oral orifice, can be applied in cases of masseteric and retromasseteric fistulae only with extreme difficulty, and it is generally agreed that its use is practically limited to the treatment of buccal fistulae.

The method of isolation of the proximal portion of the duct and its re-implantation farther back is an operation of great delicacy, the more difficult of execution the more posteriorly the fistula lies. This is also true of plastic methods of reconstruction of the duct by means of flaps taken from the skin or mucous membrane.

Arrest of the parotid secretion has been effected either by excision of the gland or by closure of the duct at the site of the fistula, followed by compression of the gland or the injection of caustic fluids into the duct itself; or by excision of the secretory nerves. Excision of the gland has the disadvantages of technical difficulty and the danger of injury to the facial nerve; and the methods involving closure of the duct are liable to grave inflammatory complications in all cases where the possibility of infection of the salivary passages is present.

Leriche's operation of excision of the secretory fibres of the auriculo-temporal nerve is carried out as follows: A small incision is made under local anaesthesia, running vertically midway between the tragus and the zygomatic tubercle and about 3 cm. in length; the pulsation of the artery serves as a guide to the position of the nerve, which is readily isolated and traced down to the parotid gland; gentle traction with forceps is then applied to its central portion, by which means a length of 3–4 cm. of the nerve is brought into view, including the bifurcation of the nerve at the middle meningeal artery; the exposed portion, which includes the secretory branches, is then excised.

Leriche found that, after excision, secretion ceased the same day. On the following day it returned, but in diminished amount, and only during the ingestion of food. On the 5th or 6th day it ceased entirely. The subsequent changes occurring in the gland have been studied experimentally by Ferrarini. The experiments were made in dogs and the results showed: (1) Diminution in volume amounting to one-third of the weight of the gland in the course of two months, with arrest of the process after that time or even some reversal of it. (2) Simple atrophy of the secretory cells more or less widely disseminated and often varying markedly in degree in contiguous zones of the gland substance, with areas of necrosis in places. (3) Oedema and increase of the interstitial, short, however, of actual fibrosis. (4) Transitory character of these changes, which appeared to be at their maximum about 1–1½ months after the operation, and thenceforward not only failed to increase but gradually diminished.

Leriche's operation has been uniformly successful, and the only point upon which differences of opinion are likely to arise has reference to the indication for its adoption. Recently Morestin and Donati have resorted to the old method of isolation, ligature, and burying of the duct in the tissues, an operation which is, according to these authors, relatively easy and results in definite cure. Morestin has treated thirty-two cases by this method. Ferrarini points out, however, that many cases of parotid fistula, and especially those met with during the war, had a marked tendency to spontaneous cure, and secondly, that in cases of old masseteric fistulae associated with deep cicatrices the operation could never be regarded as technically simple. There are, moreover, cases in which ligature of the duct is absolutely contra-indicated, as in presence of sepsis, actual or probable, of the duct or the gland itself. It is precisely in such cases, in which ligature of the duct is to be avoided or presents too great difficulty, that the operation of Leriche is indicated. Probably no one method can be regarded as the 'method of choice' in treating parotid fistulae, but, according to Ferrarini, the surgeon should restrict his choice to the following: Ligature after complete isolation of the duct in cases certainly free from infection and not associated with abundant cicatrices; puncture, with the formation of an internal orifice, in cases of buccal fistulae; excision of the nerve in infected fistulae, masseteric fistulae, and old adherent retromasseteric fistulae.

Ferrarini's own method, the practicability of which he has proved experimentally, consists in ligature of the duct followed by the direct inter-parenchymal anastomosis between the parotid and submaxillary glands, whereby the parotid secretion becomes evacuated through the duct of Wharton. The operation would be indicated in the same class of cases as those requiring Leriche's operation, which is, however, superior to it. Ferrarini suggests that it may still be found worthy of trial in cases of bilateral fistulae, which occasionally occur, and in which Leriche's operation, if applied to both sides, would result in a total abolition of the parotid secretion. T. W. P. L.

Silvestrini, L. Ricerche sperimentali sulle modificazioni del tessuto epatico in seguito all' asportazione della milza. [**Changes in the liver after splenectomy.**] *Arch. ital. di chir.*, 1920, **2**, 165.

Foà has already shown that removal of the spleen is followed by the appearance of a lymphocytic exudate around the portal venules of the liver, and he regarded the change as compensatory. Silvestrini carries the investigation a stage farther. His experiments, thirty-two in number, were made on rabbits, the animals being killed at intervals varying from a few days to two years after splenectomy. In no instance was any compensatory enlargement of the lymphatic glands observed, nor the formation of accessory spleens; on the other hand, the liver showed a slight increase in weight. The development of lymphocytes became evident on the eighth day after splenectomy; at first in the form of small isolated groups in close relation with the portal vessels, later as a perivascular zone completely ensheathing those vessels. Gradually increasing in extent during the following weeks, the deposit invaded the entire interlobular connective tissue, and subsequently made its appearance in the lobules themselves. In the latter situation the lymphocytes were arranged in small circular groups among the hepatic cells, and from the sixth to the eighth month new-formed blood-vessels and connective tissue could be distinguished within the nodules, leading to the formation, in Silvestrini's opinion, of a true lymphoid tissue. The connective tissue formed a fine network enclosing ordinary lymphocytes in its meshes, together with other cells showing evident signs of multiplication as normally met with in the so-called 'germ-centres', and a single vessel was usually present in the nodule as in the normal Malpighian follicles. In somewhat later stages red blood corpuscles, pigment, and degenerated polymorphs could be detected. Silvestrini concludes that these nodules represent a partial splenization of the liver.

The hepatic cells undergo no permanent alteration. A transitory change occurs in the form of diffuse cloudy swelling, and at the sites of deposition of the nodules some of the cells undergo atrophy, but the functional integrity of the liver is uninfluenced. T. W. P. L.

Avoni, A. Su di una cisti cutanea traumatica. [**Implantation dermoid.**] *Arch. ital. di chir.*, 1920, **2**, 135.

Fourteen years previously the patient had been dragged behind a cart for several yards. The upper third of the left thigh, at its outer part, was excoriated and bled slightly, and subsequently became swollen and ecchymosed. A few days later three litres of blood were drawn off. The injury caused little trouble for thirteen years, when a small firm swelling appeared at the inner side of the thigh in its upper third. A month later the patient, during exertion, experienced sudden acute pain in the swelling, which thenceforward gradually increased to the size of a foetal head. Pain ceased, but the swelling caused inconvenience from its size. On examination, the original external swelling was still well marked (15 × 6 cm.), and was separated from the inner by a groove corresponding in position to the sartorius muscle; fluctuation could be obtained in both, but not by transmission from one to the other. The cysts were enucleated through incisions over their most prominent parts; they contained 'coffee-grounds' fluid and communicated by a narrow opening. On microscopical examination the cyst-wall showed the structure of true skin: stratified epithelium, papillary layer, and corium with sebaceous and sudoriferous glands. T. W. P. L.

NEUROLOGY

Sherrington, C. S., and **Leyton, A. S.** **Observations on the excitable cortex of the chimpanzee, orang-utan, and gorilla.** *Quart. J. Exper. Physiol.*, 1917, **11**, 135.

This important paper contains a more detailed account of Sherrington and Leyton's investigations on the 'motor cortex' of anthropoids than was given in their well-known preliminary papers of 1901–2. It embodies the results of the examination of the excitable cortex of 22 chimpanzees, 3 orangs, and 3 gorillas. A paper so full of the most significant observations and containing so many richly suggestive conclusions is not readily reviewed and should be consulted in the original. Read in conjunction with Head's work upon sensation and the cerebral cortex (*Brain*, 1918, **41**, 57), it forms a signal advance in our knowledge of the physiology of the cerebral cortex, reached by converging lines of investigation, while, regarded purely from the point of view of the clinician, it throws much valuable light upon the phenomena of cerebral paralyses in man.

The excitable motor cortex (*precentralis motor field*) in the three species of anthropoid examined embraces the free surface and a large part of the sulcal or buried surface of the ascending frontal convolution. The area thus delimited by faradic stimulation corresponds with Campbell's histologically differentiated precentral cortex. While its posterior limits are sharply defined by the fissure of Rolando, its interior border is not thus sharply defined and is a function of several physiological factors to be mentioned. The responses obtained by stimulation show a characteristic instability, which is due to the physiological state at the moment of stimulation of the point under investigation. This in its turn depends on the facilitating influence of immediately precurrent stimulations of this or of adjacent points. Thus there are seen under various circumstances facilitation, deviation, or even reversal of the response first obtained. In addition to this physiological variation, there are fine differences of minute localization from hemisphere to hemisphere in the same individual, and also from one individual to another.

The post-central convolution is inexcitable even to strong stimulation, though closely preceding stimulation of the motor cortex at the same level often gives rise to an 'echo response' on subsequent stimulation of the post-central convolution.

Eye-opening and eye-ball movements are not represented in the precentralis field as primary movements, but can be elicited from a considerable area of the posterior ends of the second and third frontal convolutions, and also from the occipital pole. In both these situations the movements are slower and more deliberate than typical precentral field responses, require stronger stimuli, and can be obtained from a series of discontinuous spots only. The responses are bilaterally symmetrical, in which respect also they differ from precentral field responses, and consist as far as eye-ball movements are concerned in conjugate deviation to the opposite side, with occasional convergence.

Bilateral symmetry of response from the motor cortex proper is exceptional, and even jaw movements are unilateral.

Paralyses resulting from localized ablations of the excitable cortex. By the excision of carefully delimited areas of the motor cortex, complete and segmental monoplegias and hemiplegia were produced. The striking feature of the two former is their ephemeral nature and the incomplete degree of the initial paralysis. Six weeks usually sufficed to produce complete recovery, even of fine movements. Successive ablation of the corresponding post-central and the crossed motor cortex showed that the restoration of function was not due to taking over of function by these parts of the cortex. As to the mechanism of recovery Sherrington is silent.

It is of considerable interest to clinical neurologists that after the ablation of a given area of motor cortex, certain movements previously innervated from this area are unobtainable as primary movements. However, stimulation of intact motor cortex immediately adjacent to the excised area will still evoke these as secondary movements. The occurrence of voluntary synergic movement in muscles no longer capable of acting as prime mover is a familiar phenomenon in cortical paralyses and is presumably akin in origin to this experimental finding.

A study of the resulting pyramidal tract degenerations by the Marchi method shows a rough functional topography of the pyramidal fibres in cerebral peduncle, pons, and even in the cord, though in the two latter there is much overlapping. From peduncle downwards into the cord the leg fibres appear to lie laterally to those of the upper limb. A point of some therapeutic interest is that the application of local warmth or cold to the scalp rapidly affects the temperature of the subjacent cortex over a range of as much as 10° F.

The function of the motor cortex. As to the nature of the response obtained by stimulation of the motor cortex, Sherrington and Leyton find that an enormous number of localized, isolated, and perfectly co-ordinated movements are obtained. They appear to be fractional parts of larger movement complexes, and their purpose is readily seen when they are compounded into these more ample movements. It seems as though the motor cortex can synthesize an infinite number of purposive movements from these constituent elements and the authors conclude that 'the motor cortex is *par excellence* a synthetic organ for motor acts'. It selects, breaks up, and combines the various simpler movements represented in the bulbo-spinal motor mechanisms and is therefore both an analytic and synthetic mechanism; it is 'an organ for synthesis of movements—and postures—on a vast scale'.

As a general conclusion from their ablation experiments, Sherrington and Leyton consider that the animals showed a normal forerunning idea of the movement intended, and this appeared to be developed as easily and definitely as before the production of paralysis. The animal's surprise and unfulfilled expectation when the limb failed to act normally indicates 'a defect in motor execution rather than in the mental execution of the act, raising the question whether the function of the part of the cortex ablated in such cases be not indeed infra-mental'. F. M. R. W.

Dandy, W. E., and **Blackfan, K. D.** (1). **Internal hydrocephalus: an experimental, clinical, and pathological study.** *Am. J. Dis. Child.*, 1914, **8**, 406.

Dandy, W. E., and **Blackfan, K. D.** (2). **Internal hydrocephalus: second paper.** *Am. J. Dis. Child.*, 1917, **14**, 424.

Blackfan, K. D. **The early recognition of hydrocephalus in meningitis.** *Am. J. Dis. Child.*, 1919, **18**, 525.

Much of the experimental work described in the opening section of

Dandy and Blackfan's first paper has, since its appearance (1914), been carried farther and with more conclusive results by Dandy and other workers, and need not therefore be described here. Thus Dandy's work on the experimental production of hydrocephalus has been reviewed in *Medical Science* (1920, **1**, 511). While the observations of Weed and others have carried our knowledge of the pathways of absorption of cerebrospinal fluid past the point at which it was left in the present paper, and this work also has been reviewed in *Medical Science* (1920, **3**, 160).

However, some of their observations upon the conditions underlying the formation of cerebrospinal fluid are of interest. Thus, they found that compression of the jugulars rapidly and notably increased the production of the fluid, while intravenous injections of various drugs and gland extracts (amyl nitrite, pilocarpin, extract of choroid plexus, anterior and posterior lobe pituitary extracts) has relatively little stimulating effect. They then endeavoured to determine the presence of various drugs in the fluid after intravenous injections, but found that urotropin and sodium salicylate alone passed the choroid plexus and reached the fluid. This fact they regard as indicating a selective and discriminating cellular activity of the choroid plexus, rather than a filtration process. They say: 'It is evident that a mechanism which can prevent the passage of certain substances into the cerebrospinal fluid must play a very important rôle in the prevention of the haematogenous transmission of infections to the central nervous system, and, for the same reason, when affections of the central nervous system exist, they are correspondingly refractory to remedies conveyed by the blood.'

The method employed by them to determine the mode of absorption of cerebrospinal fluid consists in the replacement of a quantity of this by phenolsulphonephthalein, which is readily absorbed and as readily excreted by the kidneys. 6 mg. of the drug in 1 c.c. of neutral solution were injected into the cisterna magna of dogs through the occipito-atlantal membrane. The time of its appearance in the urine and the quantitative output were determined by a colorimetric method. In this way from 60 per cent. to 90 per cent. of the drug is recoverable in the urine. They conclude that the cerebrospinal fluid is completely absorbed and renewed at least every six hours. They found no evidence that any important amount of the drug, and therefore of the cerebrospinal fluid, found its way into the thoracic duct, and they conclude that the lymphatics take no part in this process, but that absorption takes place directly into the blood, and this from the entire subarachnoid space. Finally, they observe that the normal balance between the production and the absorption of the fluid depends upon an adequate communication between the place of formation and that of absorption; namely, between the ventricles and the subarachnoid space. This communication is by means of the three foramina of Magendie and Luschka. At this point the study of the mechanism of production of hydrocephalus is approached, for when phenolsulphonephthalein is introduced into the ventricles it appears normally in the urine within seven minutes. Conversely, when the drug is introduced into the spinal subarachnoid space, it rapidly makes its appearance in the ventricular fluid, thus demonstrating the normal presence of free communication between these spaces. By such a double introduction of the drug into the human subject in suspected cases of hydrocephalus, Dandy and Blackfan were able to determine the patency or occlusion of foramina. In normal subjects the drug appears in the urine twelve minutes after its introduction into the ventricles, and eight minutes after injection into the spinal subarachnoid space. If an obstruction exists at the foramina, phenolsuphonephthalein does not appear in the spinal fluid or in the urine. By this means they were able to differentiate two types of internal hydrocephalus: *obstructive* hydrocephalus in which the foramina were blocked, and *communicating* hydrocephalus in which they were more or less patent.

The essential feature of obstructive hydrocephalus is an absence of communication between the ventricles and the subarachnoid space. This they demonstrated clinically by the phenolsulphonephthalein test in seven cases, and confirmed *post mortem* in five. In three of these the obliteration of the foramina was a sequel of meningitis and in the remaining two there were developmental defects in the aqueduct of Sylvius, which was not patent.

In the obstructive type, the passage from ventricular system to subarachnoid space is more or less free as determined by the passage of phenolsulphonephthalein from one to the other, but the absorption of cerebrospinal fluid into the blood from the subarachnoid space is greatly delayed and diminished. This diminished absorption is the cause of the hydrocephalus. They attribute this defect to adhesions obliterating the basal cisternae. They examined one specimen of this type from a case of congenital hydrocephalus, presumably the result of an intra-uterine meningitis. The foramen of Luschka was freely open, but there was no cisterna for the reception of the fluid.

The only satisfactory clinical means of differentiating these two types and the intermediate types which probably exist is the phenolsulphonephthalein test, though sometimes information of value may be obtained by lumbar puncture, for in obstructive hydrocephalus relatively little fluid can be obtained in this way, compared to the abundance obtained in communicating hydrocephalus. In both types the essential cause of the condition appears to be *diminished absorption of cerebrospinal fluid*, normal production being maintained. In the first type (obstructive) the fluid is entirely shut off from the absorptive surface; in the second, the absorptive surface is partly obliterated, and the fluid is prevented from passing forward through the tentorium (as Dandy's later work has shown) to the large absorptive surface over the convexity of the hemispheres (c.f. Weed's work).

In their second paper, the authors present further pathological evidence of the existence of these two types of hydrocephalus. In four brains with communicating hydrocephalus, adhesions were found completely surrounding the brain and between brain and tentorium at the same level.

As a result of their clinical and pathological investigations, Dandy and Blackfan conclude that the majority of cases of hydrocephalus are due to meningitis. A hydrocephalus of short duration may follow tuberculous or pneumococcal meningitis, but chronic hydrocephalus follows meningococcal meningitis only. Pathological examination reveals signs of meningitis in both congenital and acquired varieties of hydrocephalus. This is true of both communicating and obstructive hydrocephalus. Congenital absence or obliteration of the aqueduct of Sylvius is another cause, while in adults tumour is frequently responsible.

In three cases of congenital hydrocephalus with meningocele there were marked evidences of meningitis; and Dandy and Blackfan regard both conditions as due to a single cause. It is known that the removal of a meningocele may be followed by symptoms of hydrocephalus, and they think that in this case the absorptive surface provided for the cerebrospinal fluid by the sac may just have sufficed to maintain equilibrium between the processes of production and absorption of the fluid, and that before removing a meningocele the phenolsulphonephthalein test should be employed to determine the efficiency of the subarachnoid absorptive surfaces. If this is definitely impaired, as manifested by delayed and diminished appearance of the drug in the urine, the sac should be left.

In the third paper, Blackfan discusses the possibility of the early diagnosis and differentiation of the forms of hydrocephalus in meningitis by means of the phenolsulphonephthalein test, and by means of ventricular puncture and replacement of fluid by air and subsequent radiography of the ventricles (Dandy; c.f. *Medical Science*, 1920, **1**, 511).

A practical result of these investigations, according to Blackfan, is that when obstructive hydrocephalus is diagnosed, antimeningococcic serum should be injected into the ventricles, and with communicating hydrocephalus into both ventricles and subarachnoid space (by lumbar puncture). Whether the pathological investigations recorded in these three papers have as yet a practical value equal to their theoretical interest may perhaps be questioned, as also may Blackfan's statement that these various tests add nothing to the severity of treatment, and do not demand any unnecessary operative procedure. A further communication is promised upon the operative results of a series of cases. F. M. R. W.

VOGT, C. u. O. Zur Kenntnis der pathologischen Veränderungen des Striatum und des Pallidum und zur Pathophysiologie der dabei auftretenden Krankheitserscheinungen. [**On pathological lesions in the corpus striatum and their symptomatology.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.* (Ref.), 1920, **21**, 330.

In a preliminary paper, which has been already reviewed in *Medical Science* (1920, **1**, 436) the Vogts differentiated four types of lesion in the striatum and described their appropriate symptoms. In the present paper, which is not obtainable in the original, this classification is considerably elaborated and the functions of the two parts of the corpus striatum (caudate nucleus and striatum on the one hand, and the globus pallidus on the other) are analysed. There are five sections in the paper. The first deals with the essential anatomical details of what they consider the primitive motor mechanism of the nervous system. This has not undergone any fundamental modification in man, as compared with the apes, on account of the assumption of the upright posture and the development of speech in the former, and the corpus striatum has more or less the same value in each. Among the important anatomical characters they mention are the absence of any direct pathway between the corpus striatum and the cerebral cortex, the well-developed fibre connexion between striatum and pallidum mainly from the former to the latter, the descending paths from the pallidum to the subthalamic region on both sides of the brain and the presence of a definite pathway from thalamus to pallidum.

In the second section they enumerate the various syndromes of the corpus striatum and their corresponding pathological bases.

(1) **Status marmoratus** (état marbré) in which there is loss of nerve

cells in the striatum, with a corresponding secondary degeneration of strio-pallidal fibres. Clinically, the picture is one of spastic paraplegia with athetosis and choreiform movements and a 'pseudo-Babinski reflex', general limitation of movement ('Bewegungsarmut') and a general resemblance in some instances to pseudobulbar paralysis.

(2) **Status dysmyelinatus,** in which there is progressive degeneration of efferent fibres from striatum and pallidum to the thalamus and subthalamic region. Clinically, there is progressive athetosis and rigidity, developing in early infancy.

(3) **Status fibrosus of striatum,** in which there is a progressive selective necrosis of nerve-cell bodies in the striatum, with persistence of their processes, and some degeneration of strio-pallidal fibres. The clinical correlate is progressive bilateral chorea.

(4) **Non-progressive status fibrosus** (part of Bielschowsky's cerebral hemiatrophy), in which there is a partial status fibrosus of the striatum, and clinically spastic paralysis.

(5) **Progressive total necrosis of the striatum** manifested clinically as torsion spasm (see *Medical Science,* 1920, **2**, 67), with general muscular rigidity, disturbances of articulation, limitation of movement, and forced laughter and weeping.

(6) **A cystic condition** of the head of the left nucleus caudatus and adjacent part of the putamen, manifested clinically as a right-sided chorea.

(7) **Focal gliosis of striatum with diffuse vascular changes** in the brain. There is athetosis and rigidity, greatly increased by peripheral or by psychical stimuli.

(8) **Status disintegrationis,** in which there are diffuse degenerative changes in both cells and processes, particularly in the caudatus. Here also there are vascular changes. Clinically, there is tremor and rigidity and forced laughter and a mask-like facies.

In the third section the symptoms are discussed singly. The characters of the rigidity alone demand a note here. They include the equal and simultaneous involvement of both agonist and antagonist muscle (unlike the spasticity of pyramidal tract lesion). This tends to the fixation of attitudes and to the impeding of free movement.

In the fourth section the physiological significance of these symptoms is the subject of analysis. The authors conclude that the striatum stands to the pallidum in the same relation as the cerebral motor cortex does to the motor nuclei of the tegmentum and brain-stem. They draw an analogy with the results of a cortical lesion as follows: immediately after an acute cortical lesion, there is a transient phase of 'cortical hyperkinesis', or of cortical irritation manifested as clonic muscular contractions; there is a second phase of flaccid paralysis, due to shock effect upon subcortical centres, and a third and permanent residual phase of subcortical hyperkinesis—that is, of spastic paralysis, in which the spasticity is due to over-action of released subcortical centres. This is the Jacksonian principle long familiar to English neurologists. The striatum has a similar inhibitory and controlling action on the pallidum and subpallidal centres. The first phase of a striatal lesion would result in the production of striatal hyperkinesis manifested as movements normally produced by the activity of the striatum (what the clinical manifestation of these may be is not clear); the second phase cannot be identified apparently from the presence of substrial hyperkinesis, but on theoretical grounds this might be expected to be a loss of primary automatisms manifested as defective co-ordination of speech and locomotive movements. They regard both athetosis and choreiform movement as substrial hyperkinesis, hence the tendency to athetosis in congenital striatum lesions. The relatively late myelination of the striatum fibres as compared with those of the pallidum may account for the similarity of the movements of the newly born to those seen in striatum lesions. (This is to add yet another comparison to the numerous ones already invoked with regard to infantile movements.)

The effect of a thalamic lesion is to cut off 'affective' impulses which normally travel towards the striatum by cortico-thalamic fibres. From the thalamus association fibres pass on these impulses to the pallidum and striatum. The result is an over-activity of the released pallidum in response to sensory, emotional, and other stimuli. The pallidal symptom rigidity is due to release of subpallidal centres, but while the striatum syndrome may be unilateral (athetosis, &c.), the pallidal syndrome (rigidity) must be bilateral, since the descending connexions of the pallidum are bilateral.

The fifth section deals with the general functions of the striatum and pallidum. They are centres for 'primary automatisms'. In the first months of life the pallidum alone controls these; later the striatum exercises a controlling and restraining action and becomes the centre for all expressional and emotional movement complexes, for automatic associated movements, and for defensive reflexes.

It may be added, in conclusion, that it is extremely difficult to assess the value of the authors' conclusions, or even to gauge their meaning from the condensed abstract of their paper, which is alone available in this country at present. F. M. R. W.

Spiller, W. G. Acquired double athetosis (*Dystonia lenticularis*). *Arch. Neurol. & Psychiat.*, 1920, **4**, 370.

Spiller reports a case of pure double athetosis with rigidity dating from early childhood and persisting until death at the age of 53. The essential lesion was in the lenticular nucleus and was bilaterally symmetrical. The putamen was practically completely disintegrated, while the globus pallidus and caudate nucleus were somewhat atrophied. There were no noteworthy changes in the cerebral cortex.

In discussing the differential diagnosis between progressive lenticular degeneration (Wilson) and pseudo-sclerosis (Westphal-Strumpell), Spiller draws attention to a point of some importance in estimating the physiological significance of the so-called corpus striatum syndromes named above and to which 'torsion dystonia' or 'torsion spasm' (*Medical Science*, 1920, **2**, 67) has now been added. While Wilson found a pure lenticular nucleus lesion in his cases, more recent investigations have indicated the presence of widespread changes in the cells of the cerebral cortex, while in the case of pseudosclerosis, which German writers now regard as the same disease as that described by Wilson, Hösslin and Alzheimer have found widespread changes in the brain, particularly in the basal ganglia, subthalamic region, pons, and dentate nucleus.

The latest investigations, recently published by Spielmeyer, also tend to confirm the view that the lesions underlying the corpus striatum syndromes are not confined to these structures, and cannot therefore be regarded as system diseases. That the latest experimental work upon the corpus striatum, namely, that of Wilson (*Brain*, 1913), should have given completely negative results in the sense that neither stimulation nor destruction of these nuclei in apes produced any disorder of the motor system, is significant in the light of these pathological observations.

Both aspects of the problem indicate the great caution needed in accepting the elaborate clinical and physiological analysis of corpus striatum diseases and functions put forward by the Vogts and reviewed in the present number of *Medical Science*. F. M. R. W.

Westphal, A. Beitrag zur Lehre von der stationären Tabes. [**A case of non-progressive tabes.**] *Deutsche Ztschr. f. Nervenheilk.*, 1918, **60**, 80.

Westphal reports a case of tabes in a woman, who was known to have had absent tendon reflexes for 27 years before her death at the age of 60. During the whole of this period there was no disability of any kind associated with these signs, which constituted the sole objective manifestations of a nervous lesion. At no time were there pupil changes, ataxy, sphincter defects, subjective or objective sensory changes, a positive Wassermann reaction, or any abnormality in the cerebrospinal fluid. It seemed probable, therefore, that the case was one of congenital absence of the tendon reflexes, of which a few have been recorded, rather than a syphilitic nervous lesion. No positive diagnosis of tabes could therefore be made during life. In 1917 the patient's general health failed rapidly and she died. On examination the spinal cord appeared somewhat shrunken, and on section showed a distinct grey degeneration of the posterior columns. Examined by the Weigert-Pal method, the typical tabetic degeneration in the posterior columns was seen, though it was at no level profound.

The case may perhaps be regarded as an example of 'monosymptomatic' or 'rudimentary' tabes, and it indicates that the diagnosis of congenital absence of the tendon reflexes as a 'stigma degenerationis' is one that should be made with caution. F. M. R. W.

Netter, A. L'encéphalite léthargique. [**Lethargic encephalitis.**] *Presse méd.*, 1920, i, 193.

In the course of a general review of the present state of knowledge of this disease, more particularly as it has been observed in France, Netter, one of the foremost observers in that country, raises some questions of theoretical and practical interest.

Among these is his grouping of the 'delirium of word and action', the choreiform restlessness, the convulsions, and the 'secousses myocloniques', which have been such striking features of lethargic encephalitis during the past winter, as irritative phenomena indicating the minimal effect ('atteinte minime') of the virus on the nervous system.

When more intense, its action produces paralytic phenomena. The symptoms in question have been among the most obscure nervous manifestations of lethargic encephalitis, but it is doubtful whether Netter's explanation is really applicable to the facts. He has pointed out elsewhere in this connexion that such poisons as alcohol, lead, and the virus of rabies may produce either irritative (convulsive) or paralytic phenomena from their effect upon the nervous system, but there is no reason to suppose that this depends primarily upon the intensity of the poisoning.

In the case of the disease under discussion there are what seem conclusive reasons for rejecting this view. In the first place, rapidly fatal cases have been recorded in which none but irritative symptoms were observed (Sicard's myoclonic encephalitis and cases with choreiform manifestations), and in which, therefore, Netter's view is not tenable. Moreover, it is a striking fact that the parts of the nervous system which appear to be irritated by the virus of the disease are not those which we find paralysed. The paralytic symptoms are remarkably restricted and selective in their topography. The irritative symptoms, on the other hand, are quite non-selective and appear to arise from neurones of every physiological level, or, speaking anatomically, every part of the nervous system indifferently may be the seat of irritative manifestations. In its dual action upon the nervous system, therefore, the virus of lethargic encephalitis appears to have a distinct and characteristic incidence in each case. This is not to be explained by Netter's hypothesis, and it seems probable that we must look to the nature of the virus itself for the explanation of this double action and double incidence.

Netter has noticed enlargement of the salivary glands and profuse salivation as common symptoms of the disease. He compares it with rabies in this respect, where the virus may often be found in the saliva. If the comparison is borne out in fact, the saliva of patients must be a source of infection. Netter's practical conclusion is that by means of pilocarpin or jaborandi he causes sialorrhoea and thus aids in the clearing out of the virus.

In severe cases he advocates the use of subcutaneous injections of turpentine to produce 'fixation abcesses'.

The descriptive and historical portions of the paper contain nothing not now familiar to English readers. F. M. R. W.

COMMITTEE UPON INJURIES OF THE NERVOUS SYSTEM. The diagnosis and treatment of peripheral nerve injuries. *Medical Research Council, Special Report Series*, 1920, **54**.

The Committee state that the object of the report is to enunciate the general principles of treatment, and to indicate the variations demanded by the special physiology and pathology of each of the more important nerves. No attempt is made to discuss the many academic and scientific questions which are associated with the physiology and pathology of the peripheral nervous system, nor to lay down any hard and fast rules in regard to procedure which should be adopted in the treatment of nerve injuries, but their aim has been to collect and propagate the knowledge which has been gained by a number of observers as the result of their experience during the war. A report drawn up by this committee of nine members, and on the lines so described, must have many advantages that the recorded experience of a single observer will lack, and the present account of peripheral nerve injuries is both comprehensive and systematic. F. M. R. W.

VERZÁR, F. Reflexumkehr (paradoxe Reflexe) durch Ermüdung und Shock. [**Reversal of reflexes (paradox reflexes) in fatigue and shock.**] *Arch. f. d. ges. Physiol.*, 1920, **183**, 210.

The investigation (the outcome of observations on 'nerve shock' in soldiers) was carried out on frogs, the reflex chosen being the flexor response of the hind limb in the brainless animal. Inversion of the reflex was obtained (in response to stimulation of the skin of the foot) by increase of stimulus, by fatigue, and by loss of blood, &c. These phenomena are the result of fatigue of the synapses of intercalary neurons; by applying the releasing stimulus to a different area of skin, the extensor response vanishes and the normal reflex reappears. C. L. E.

PATHOLOGY AND BACTERIOLOGY

Cecil, Russell L., and **Blake, Francis G.** **Studies on experimental pneumonia. VII. Treatment of experimental pneumococcus Type I pneumonia in monkeys with Type I antipneumococcus serum.** *J. Exper. M.*, 1920, **33**, 1.

Abstracts of the important work of Cecil and Blake on experimental pneumonia have already been given (vide *Medical Science*, 1920, **3**, 63). In their present—the seventh—communication they deal with the curative value of antipneumococcus Type I serum on Type I pneumonia evoked in monkeys (*Macacus syrichtus*) by the intratracheal injection of living cultures. Clinical histories are presented of the results of injection of curative serum both early and late in the disease, as well as the results after injection of normal horse serum. When the results are compared with the fate of control animals it is evident that intravenous injection of Type I antipneumococcus serum frees the blood quickly and permanently from pneumococci, shortens the course of the disease and moderates its severity. The best results were obtained by early injections which were repeated several times. Normal horse serum had no curative effect. It would thus appear that the beneficial results claimed for antipneumococcus serum-therapy rests on a sound experimental basis, especially with reference to pneumococcus Type I. The negative or imperfect results which have occurred in the hands of some are put down by the present authors to (1) incorrect determination of the type of pneumococcus; (2) late administration of the remedy; (3) insufficient doses at too infrequent intervals. Reference is made to an epidemic of pneumococcus Type I pneumonia among negro troops in 1918. In spite of serum treatment the mortality was 34·5 per cent. instead of a mortality of 7 per cent. in cases treated in the Rockefeller Institute. Inquiry showed that two-thirds of the cases did not receive serum until 48 hours or more after admission, and one-half of the cases were not treated specifically until at least the fourth day. In addition, the doses were too small and were given at too infrequent intervals. W. B.

Glover, J. A. **Some deductions from a series of 243 military cases of cerebrospinal fever in the London district with regard to the variations in the therapeutic potency of serum.** *J. Roy. Army Med. Corps*, 1920, **34**, 499.

The chief factors governing the success of treatment were practically the same during the years of war in London except the therapeutic serum, and the author attributes the varying mortality to differences in the quality of the sera used. He discards the possibility of variation in the virulence of the disease, because the mortality dropped in the middle of an epidemic upon the introduction of a new serum. A good serum is to be distinguished from a bad by the fact that it will protect against 1 minimal lethal dose of meningococcus ‘endotoxin’. P. F.

Mackie, T. J. Variation in agglutinability of bacteria associated with variation of cultural characters. *Brit. J. Expėr. Path.*, 1920, **1**, 213.

When *B. vesiculosus* was grown in agar containing a small quantity of brilliant green, colonies of different types developed, the difference being maintained in subculture. These colonies reacted in different degrees to an agglutinating serum prepared against the original strain, one type being five times more agglutinable than the original. This altered agglutinability did not depend upon capsules. P. F.

Jötten, K. W. Beziehungen verschiedener Gonokokkenarten zur Schwere der Infektion. [**The relation of diverse races of gonococci to the severity of the infection.**] *München. med. Wchnschr.*, 1920, **67**, 1067.

Working in Kruse's laboratory, in Leipzig, the author made a study of the agglutination, opsonic, bacteriotropic, bactericidal, and complement-fixation reactions, as well as the toxicity on mice of 27 strains of gonococci. By agglutination and complement-fixing tests he found that they fell into four groups A, B, C, D. Groups A and B were more resistant in phagocytic experiments and also manifested greater toxicity when injected into mice. In addition, they appeared to have produced serious consequences in the patients who harboured them. W. B.

Colebrook, L. The mycelial and other micro-organisms associated with human actinomycosis. *Brit. J. Exper. Path.*, 1920, **1**, 197.

(1) Cultures of mycelial organisms were obtained from the granules of twenty-four cases of human actinomycosis. Twenty-one of the twenty-four strains conformed in their general characters to the anaerobic type described by Wolff and Israel (*Actinomyces bovis*), and later, in greater detail, by Homer Wright; two strains were also anaerobic organisms, but with slightly different cultural characters; and one was a quite different, aerobic type.

(2) All strains of *Actinomyces bovis* which were tested showed coarse agglutination with the serum of heavily infected patients. The serum of rabbits inoculated with the organism also gave a strong agglutination reaction.

(3) The current hypothesis that actinomycosis is directly conveyed to man from vegetable sources or from soil is held to be probably false. Certain evidence is put forward which suggests that the organism is a common inhabitant of the human alimentary tract.

(4) Attention is called to the fact that, in addition to the mycelial feltwork always found in actinomycotic granules, there are frequently immense numbers of minute Gram-negative cocco-bacilli. In 80 per cent. of the cases these organisms have been found at some period of the disease ; and in about a dozen instances they have been cultivated on artificial media. They are of unfamiliar type, and have not, so far as is known, been met with in any other circumstances. It was proposed by Klinger, who reported the cultivation of similar organisms from four cases of actinomycosis in 1912, to apply to them the name *B. actinomycetum comitans*. This name is here employed. The association of *B. actinomycetum comitans* with actinomyces in the granules is discussed, but no satisfactory explanation has been arrived at. The findings are somewhat suggestive of a genetic relationship between the bacillary organism and actinomyces, analogous to that which Dunbar claimed to have demonstrated in the case of cholera-like vibrios and algae.

P. F.

Caldera, C. Contributo sperimentale allo studio eziologico dell' ozena. [**Experimental investigation on the aetiology of ozoena.**] *Ann. d'ig.*, 1920, **30**, 168–71.

All experiments had a negative result, and the author therefore comes to the conclusion that ozoena is a syndrome connected with the lymphatic temperament of the patients, and that the 'bad odour' is due to bacteria, none of which, however, can be considered as the specific agent of the disease. C. d. F.

Neufeld, F. Zur Frage des Influenzaerregers. [**The aetiology of influenza.**] *Deutsche med. Wchnschr.*, 1920, **46**, 957.

This review indicates a tendency on the part of German authors to return to a more 'academic' view of the cause of influenza than has been apparent for some time.

'Experiments performed up to now do not appear to me to supply a certain proof of filter-passing viruses being the cause of influenza; on the other hand, the behaviour of Pfeiffer's bacillus is not inconsistent with what we should expect from the virus causing this disease.' P. F.

Topley, W. W. C., Platts, S. G., and Imrie, C. G. A report on the probable proportion of enteric infections among undiagnosed febrile cases invalided from the Western Front since October 1916. *Med. Res. Com., Special Report Series*, **48**, 1920.

This valuable report embodies an attempt to estimate by laboratory tests the number of infections with *B. typhosus*, *B. paratyphosus* A, and *B. paratyphosus* B among soldiers suffering or convalescent from atypical febrile disturbances, who returned home from over-seas, and chiefly from the Western Front, between October 1916 and January 1919. The main method adopted was that of repeated agglutination tests with standardized cultures, as recommended by Dreyer and his co-workers. It was hoped that confirmatory evidence might be obtained with other bacteriological methods, but owing, in all probability, to the modification of the disease by inoculation, this proved unobtainable, and the authors were driven to rely upon agglutination tests alone. In accordance with the cautious scientific spirit, which is in evidence throughout the report, they proceeded to make a preliminary investigation concerning the trustworthiness of Dreyer's method. Part II describes the results of this inquiry, which resulted favourably for the method, with the following reservations:

(1) That variations of bacterial antigen and of the resulting antibody may interfere with true standardization of suspensions made with different strains of a species.

This conclusion is based on the findings with cultures of *B. paratyphosus* A and (especially) *B. paratyphosus* B. All the experiments with *B. typhosus* spoke for complete serological uniformity in this species. It is impossible within the scope of this note to discuss these experiments adequately, but certain points may be noted in this connexion.

First, that the standard cultures employed were being turned out in great bulk under the stress of war, and with very imperfect materials, for which reasons a uniform standard of excellence was not always attainable. Certain of the discrepancies between the reporter's findings and the official statements of the agglutinability factors of the various batches of cultures may be accounted for by the somewhat variable behaviour of inferior suspensions (e. g. *Para.* A, Nos. 23 and 32, were of poor quality).

Secondly, the experiments with *B. paratyphosus* B (Table XIII), which, in the author's view, speak for definite antigenic differences within this species, may well prove explicable on other grounds when further information is amassed concerning the limits of variability of subcultures of a single strain. It is to be noticed that the three subcultures of each of the strains used in Table XIII differ from each other more widely than their average differs from that of the standard cultures. Nevertheless, in the light of other recent work on the serological composition of the paratyphoid B 'groups', these experiments will, unless otherwise explained, be brought in evidence against the uniformity of the species.

(2) The authors reject the expression of results in agglutinin units, mainly as implying the existence of a definite substance called 'agglutinin'. They are, however, prepared, nay, even anxious, to standardize measurements of agglutinating power wherever scientific truth will allow; and, this being so, it is hard to understand how they can logically avoid the use of a standard unit. For no measurement can be made without some kind of unit, and general acceptance of any particular unit of measurement converts it into a standard unit. It would seem that the use of the words 'agglutinating power' in place of 'agglutinin' in the definition of the unit would meet the main part of the authors' objection.

Part III contains some valuable observations on the effects of previous inoculations upon the agglutinin curve of persons or animals inoculated again with the same bacillus.

In some cases the fall from the maximum of the curve is so slow as to be imperceptible from week to week. Important deductions are drawn as to the diagnostic significance of persistent high-level 'plateaus' of agglutination which are sometimes found in inoculated persons under examination for possible enteric infections.

The authors adopt the reasonable and attractive method of curve-plotting in which the ordinates are scaled in geometrical in place of the commoner arithmetical ratio. But in choosing between the alternative methods of joining the plotted points with straight lines, or of drawing through them a smooth curve, they prefer the former, which must always misrepresent the truth, to the latter, which sometimes misinterprets it. The difficulty could be avoided by simply leaving the points unjoined.

In Part IV are described the results of testing some 500 soldiers' bloods at intervals, with the object of detecting undiagnosed enteric infections.

The criterion employed by the authors is a rise or fall of at least 200 per cent. in agglutinating power within a period of a few weeks. In discussing this criterion and its trustworthiness they show that

(*a*) Whereas the results obtained with Dreyer's method by the American Red Cross Commission on trench fever showed variations of this magnitude, or greater, in 95 per cent. of persons tested who were undoubtedly not suffering from enteric fever,

(*b*) they themselves could find similar variations only in 8 per cent. of their cases, and nearly all of this 8 per cent. could be reasonably explained either as due to actual enteric or to technical errors.

The authors' findings, combined with those of certain other British workers, compel them to disregard provisionally the American experiments, and to accept Dreyer's system as trustworthy; though they feel that Prof. Dreyer and his school should have paid more attention to the American work. There can be little doubt that the authors' belief in the correctness of their own results is fully justified.

Applying the 200 per cent. criterion, they judged some 12 cases to be definitely enteric fever, and a further 7 to be probably enteric. In the latter group some are open to a good deal of doubt.

Since other bacteriological tests had proved almost uniformly negative (most probably in consequence of the great modification of the disease by inoculation) it was only possible to produce a small amount of indirect confirmation by showing

(1) That practically all the undiagnosed enteric cases were found in the general class of 'atypical pyrexias', of which no definite clinical diagnosis could be made.

(2) That the time-distribution of the cases conformed generally with the usual seasonal distribution of enteric fever.

(3) That the clinical histories in practically every case were in accord with the serological findings. An incidental point of no little importance is the observation that nephritis may play havoc with the regularity of agglutination curves, and so lay a trap for the unwary pathologist.

The chief conclusions of the report may thus be summarized:

(i) The technique advocated by Dreyer is admirably adopted for the purpose in view, and would seem to afford our best hope of identifying atypical enteric infections in inoculated persons.

(ii) Between October 1916 and March 1918 it is probable that between 5 per cent. and 7 per cent. of undiagnosed febrile cases from the Western Front were enterics.

(iii) Previous inoculation does not increase the tendency of an infected person to become a chronic carrier. A. D. G.

Solimano, G. Agglutinabilità e attività disintegrative quali caratteri differenziali del B. di Shiga. [**Agglutination and disintegrative biochemical activities of *B. dysenteriae*, 'Shiga'.**] *Pathologica*, 1920, **12**, 113–24.

Great difficulties may be experienced in the bacteriological identification of intestinal pathogenic germs in general, but particularly of dysentery strains. In many cases a definite discrimination is only reached by having recourse to delicate methods of investigation such as the determination of the biochemical activities of the isolated strains and of their specific agglutination reaction. The diagnostic value of these two methods has been variously emphasized by different authors, some giving more importance to the disintegrative biochemical characters, others to the agglutination reaction. Particularly with regard to dysentery bacilli, investigators have of late shown an increasing tendency to give more and more importance to the latter, especially in those cases in which agglutination occurs to end titre of high titre agglutinating sera. According to Solimano this is a disputable question, because for the identification of germs by means of agglutinating sera it is not only necessary that their specificity be so limited as clearly to show the differences between various types, but that the latter maintain unchanged the property of reacting with certain sera. Solimano points out that these two conditions do not always obtain. For instance, sera agglutinating to end titre 'Shiga' strains may, though at an inferior titre, agglutinate also 'Flexner' strains; 'Y' sera generally show a remarkable agglutinating power for 'Shiga' strains. Chick (*Lancet*, April 1916) and Mackie (*J. Hyg.*, April 1919) have also shown that a distinction between *B. dysenteriae* (Flexner), and *B. dysenteriae* 'Y' may be impossible by serological means only, in so far as strains may be met with which are agglutinated by both 'Flexner' and 'Y' sera. On the other hand, the characters of certain strains may change in course of time in so far as they may temporarily in part lose their agglutination reaction, or strains which do not agglutinate in primary culture may become agglutinable after repeated culture.

For these reasons a systematic investigation was made on 111 dysenteric strains isolated at the 'Ospedali della Galliera, Genova' during various epidemics of the disease, with a view to ascertain as far as possible the practical value of the two methods mentioned above. The results are summarized by Solimano as follows: (1) The biochemical reactions of 'Shiga' strains have a constant essential character, which must be considered as the expression of fundamental protoplasmic activities. (2) The agglutination reaction is a physical datum dependent upon special conditions of surroundings; it may remain latent for a time and then reappear. Caution is therefore necessary in expressing any conclusion on the base of this one reaction only. C. d. F.

Bastai, P. Una epidemia idrica di tifo. Valore della vaccinazione preventiva. [**On an epidemic of typhoid fever. Importance of preventive vaccination.**] *Ann. d'ig.*, 1920, **30**, 145–53.

During an epidemic of typhoid fever observations were made from which the author draws the following conclusions: (1) Recent subcutaneous inoculation of ordinary doses of antityphoid vaccine are sufficient to protect a great number of people exposed to the danger of contracting the infection. (2) Antityphoid vaccination, if resorted to after the disease has been contracted, may modify its course, but does not influence its severity. (3) One can generally accept the principle that natural immunity is practically non-existent in young people up to about 35 years of age, but it becomes considerable after 40 years of age. C. d. F.

Myers, J. T. The production of hydrogen sulphide by bacteria. *J. Bacteriol.*, 1920, **5**, 231.

Hydrogen sulphide is a widely distributed bacterial product, and for the most part is derived from the splitting of the protein of the culture media. It has also been shown by Beijerinck that certain anaerobic bacteria, e. g. *Spirillum desulphuricans*, can reduce inorganic sulphates. A number of workers have also assumed that SH_2 formation in cultures from water is proportional to the degree of pollution. In 1915 Burnet and Weisenbach showed that colonies of *B. paratyphosus* B become black when grown on agar containing lead acetate while colonies of *B. paratyphosus* A were unable to produce this effect—a fact which has been confirmed by others. The present author has made experiments to determine whether the hydrogen sulphide test as applied to potable waters is both delicate and reliable. He used a medium containing sodium chloride and Difco peptone and suspended from the necks of the flasks strips of filter paper which had been moistened with a solution of acetate of lead. Equal quantities of faeces were diluted down and inoculated into the culture medium, the amount of blackening of the lead acetate paper being recorded at various times in millimetres. No constant differences were found in the amounts of SH_2 produced by human and animal faeces. All contaminated waters gave a positive reaction and many were also positive which gave no evidence of contamination by other methods. A number of bacteria were able to split off SH_2 from Witte's peptone but not from Difco. Sodium sulphate was not reduced in any of the experiments made by the author. He also found that all strains of *B. paratyphosus* B and of *B. typhosus* produced SH_2 in twenty-four hours, while all cultures of *B. paratyphosus* A were negative. W. B.

Koch, J., and **Möllers, B.** Zur Frage der Infektionswege der Tuberkulose. [**Paths of infection in tubercle.**] *Deutsche med. Wchnschr.*, 1920, **46**, 901.

The authors studied the paths of infection in tuberculosis by infecting definite parts of the gastro-intestinal tract of rabbits with bovine type tubercle bacilli.

The small intestine was studied by injecting the bacilli directly into the lumen of the gut through a laparotomy opening. It was found that bacilli introduced in this way appeared in the blood in 1½ hours. The internal organs were also rapidly infected, as shown by guinea-pig inoculation. The bacilli are taken up by the chyle vessels and conveyed to the mesenteric glands; here some are retained while the rest pass into the blood.

In other experiments the bacilli were introduced into the stomach through a tube. It appeared, however, that most of the bacilli were destroyed by the gastric juices, because a general infection seldom followed.

Infection through the mouth was studied by injecting the bacilli through a small hole bored through a wood block which was clamped between the teeth of the animal. In this way, however, a general infection could not be obtained but only a chronic pulmonary tubercle similar to phthisis in man, and a cervical adenitis. The authors look upon this latter experiment as important as indicating a path of infection in man. P. F.

Melchior, L. Om Patogenesen af den tuberkulöse Peritonitis. [**The pathogenesis of tuberculous peritonitis.**] *Ugesk. f. Læger.*, 1919, **81**, 1665; 1713.

Melchior's investigations were made in the pathological department of the Kommunehospital in Copenhagen in the period Jan. 1, 1914–July 1, 1919. In this period the total number of necropsies was 4,572, among which there were 36 cases of definite tuberculous peritonitis. The incidence of tuberculous peritonitis was thus about 0·8 per cent. Melchior classifies his cases according to sex and age, so as to elucidate, if possible, the sex and age peculiarities of the disease. There were 7 children, 14 women, and 15 men. Among the children, all under the age of seven, there were no fewer than six with tuberculosis of the mesenteric glands. In three of these cases there was no macroscopic sign of tuberculosis in the wall of the gut. In three other cases the small intestine was the seat of tuberculous ulcers. The bronchial glands were involved in five cases. In one case only was there well-defined tuberculous infiltration of the pleurae. Melchior gathers from this meagre material that, as tuberculosis of the mesenteric glands is the most common tuberculous lesion accompanying tuberculous peritonitis, the peritonitis must be a sequel to infection through the gut or through the mesenteric glands.

In the second class, represented by 14 women at the age of puberty and upwards, the most common tuberculous accompaniment to the peritonitis was disease of the internal reproductive organs. These were involved in as many as 12 cases. In eight cases there were absolutely no signs of tuberculosis of the intestine, but in one of these there were a few caseous foci in the mesenteric glands. A characteristic feature of this class was the comparative freedom from tuberculosis of the lungs. In only four cases was there extensive pulmonary disease, and in none of these was the disease of the chronic, progressive character, typical of phthisis. The pleurae, on the other hand, were affected in most cases, and there was only one in which they were perfectly healthy. Melchior concludes that, in women, tuberculosis of the internal reproductive organs is the most important factor in the development of tuberculous peritonitis, and he draws special attention to two of his cases in which the only tuberculous manifestation, apart from the peritonitis, was tuberculosis of the internal reproductive organs. He discusses at some length the conflicting views as to the relation of tuberculosis of the peritoneum to that of the internal reproductive organs, and he concludes that the evidence in favour of the peritonitis being primary, the disease of the reproductive organs secondary, is unconvincing. In this connexion he points out that in 50 per cent. of his cases the gut and mesenteric glands were intact. This certainly does not point to spread of infection from gut to peritoneum and thence to the internal reproductive organs. His material suggests that in women the peritoneum, as Broudardel pointed out in 1865, is infected in the same manner as the pleurae in pulmonary tuberculosis.

Melchior's 15 cases of tuberculous peritonitis in men, between the ages of 17 and 76, were characterized by the complete absence of tuberculosis of the reproductive organs. This was all the more strange as tuberculosis of these organs is comparatively common. There was also no case of general miliary tuberculosis, of tuberculous meningitis, nor of tuberculosis of the urinary tract, apart from one case of miliary tubercles of the kidneys. But in as many as eight cases there was extensive pulmonary tuberculosis, and in four cases there was cirrhosis of the liver, of Laennec's type. The pleurae were diseased in practically every case. It would therefore appear that, in men, the most frequent tuberculous accompaniment to the disease of the peritoneum is pleurisy and tuberculosis of the lungs and bronchial glands. Melchior suggests that his findings may prove a useful guide to treatment; the peritonitis being traced in children and men to inoperable sources, radical cure by surgical treatment would seem unfeasible. The outlook is better in this respect for women, the primary focus of disease being situated in organs accessible to the surgeon. Melchior also suggests that his analysis helps to explain the old paradox that, while post-mortem statistics show tuberculous peritonitis to be far commoner in men than in women, operative statistics reverse this order of frequency. For the disease in women becomes clinically manifest in a greater proportion of cases. C. L.

Ottolenghi, D., Tonietti, F., e **D'Antona, S.** Recerche sull' eziologia e sulla patogenesi dell' encefalite letargica. **[Investigations on the aetiology and pathogenesis of encephalitis lethargica.]** *Atti d. r. Accad. d. fisiocrit. di Siena*, 1920. (*Gazz. d. osp.*, 1920, **41**, 512.)

Experiments were made in January of this year and are summarized by the authors approximately as follows: (1) The intracerebral inoculation of either blood or cerebrospinal fluid obtained from patients with encephalitis lethargica is almost always fatal for guinea-pigs. Intraperitoneal inoculations are less effective. (2) The disease caused by such inoculations is transmissible in series from animal to animal; it is not characterized by special symptoms and lasts generally from 7 to 30 days. (3) The brain of the infected animals shows a certain degree of congestion. In the cerebral cortex, cerebellum, and pons, foci of 'degeneration' are found. (4) In one case cultures led to the isolation of a diplostreptococcus similar to that observed by v. Viessner and afterwards by Maggiora, but the authors are very sceptical about the aetiological importance of these streptococci. (5) The virus contained in the cerebrospinal fluid from cases of lethargic encephalitis is still virulent after conservation in the dark and at low temperatures, for any number of days up to twelve. (6) Guinea-pigs may be infected by pouring a few drops of cerebrospinal fluid on their nasal mucous membrane. C. d. F.

Lurzatto, A. M., e **Rietti, F.** Appunti clinici ed anatomo-patologici sull'encefalite letargica. [**Clinical and pathological observations on encephalitis lethargica.**] *Atti. Accad. d. sc. med. e nat. in Ferrara*, 1919–20. (*Riforma med.*, 1920, **36**, 579.)

Histopathological investigations could be carried out in four out of 30 cases in which clinical observations were possible. The examination of various regions of the central nervous system revealed the well-known inflammatory lesions and perivascular infiltrations repeatedly described in this disease. In the cases studied by the authors they were more remarkable in the medulla oblongata and pons as well as in the cerebral cortex, where also 'severe lesions of the endo- and peri-cellular network' were found. All bacteriological and serological investigations were attended by negative results. C. d. F.

Azzi, A. (1). Sui fattori d'inattivazione del complemento nel sistema emolitico. [**On the inactivation of complement in the haemolytic system.**] *Haematologica* (Napoli), 1920, **1**, 126.

Azzi, A. (2). Azione degli acidi e degli alcali sul componente termostabile del complemento. [**Action of acids and alkalis upon the thermostabile component of complement.**] *Arch. di fisiol.*, 1918, **16**, 95.

In his earlier communication Azzi had shown that the three components of complement show a variable sensitivity to the action of acids and alkalis. The most sensitive is that bound to the globulins; less sensitive is that bound to the albumins; still less the third element, which is thermostabile and sensitive to cobra venom. The great sensitiveness of the first two components is proved by the fact that if separated and dissolved in physiological solution they become spontaneously altered in a very short time. This is particularly true of the substance bound to the globulins. On the other hand, they are, when united, more resistant than the thermostabile component. This last may therefore be eliminated by treating the serum not only with cobra venom, but also with HCl or NaOH of proper density.

The author has subsequently studied the question from a more general point of view, taking, however, into particular consideration the inactivation and re-activation of the complement. The results reached may be summarized as follows: The complement of güinea-pig's serum is inactivated by prolonged and energetic shaking, as well as by treatment with cobra venom, acids, and alkalis, but it is re-activated by the addition of serum warmed at 54° C. for 20 minutes. The complement inactivated by shaking is re-activated by the addition of serum inactivated by cobra venom, acids, and alkalis. But the complement inactivated by cobra venom is not re-activated by the addition of serum inactivated by acids or alkalis; and the complement inactivated by acids is not re-activated by the addition of serum inactivated with alkalis.

These and the results previously obtained taken together with the conclusions arrived at by other authors, show that guinea-pig's serum may be inactivated and re-activated by a great number of factors and in the most various ways. This is against the assumption that inactivation is due to the destruction of particular substances and that complement consists of one or more chemically definable bodies. It appears more likely that complemental activity may consist in a colloidal equilibrium easily altered by means of a great number of chemical or physical agents. Hence the wider suggestion of considering specific haemolysis not as a sort of fermentative reaction caused by a special substance but as a physio-chemical change due to the alteration of a colloidal equilibrium. C. d. F.

CARPANO, M. Sull' azione antinfettiva e sul potere batteriotropo dei sieri antistreptococcici preparati con germi viventi ed uccisi. [**On the anti-infective action and on the bacteriotropic power of antistreptococcic sera prepared with living and killed germs.**] *Ann. d'ig.*, 1920, **30**, 164–8.

The bacteriotropic power of antistreptococcic sera prepared with killed germs is about the same as that of sera prepared with living streptococci, but antistreptoccic sera obtained by hyper-immunizing animals with living germs have an 'anti-infective' (viz. protective) power certainly greater than that of sera obtained by immunization with killed germs. Hence the conclusion that there is no parallelism between bacteriotropic and protective powers, and that one cannot express any definite opinion on the protective power of a determined serum on the sole basis of its bacteriotropic properties. C. d. F.

BESREDKA, A. Essai d'épuration des sérums thérapeutiques. [**On the purification of therapeutic sera.**] *Compt. rend. Acad. d. Sc.*, 1920, **170**, 1628–9.

If one part of a dry serum is diluted with two parts of physiological solution and the mixture heated to 57°–58° C., and subsequently desiccated, one obtains again an apparently normal dry serum. This, in fact, has still its specific properties, but is insoluble in water and offers the advantage of being well tolerated by anaphylactic animals, to which it can be administered intratracheally in watery emulsion, since intravenous injection is likely to cause embolism. This emulsion, if left overnight, separates into two layers, the lower one of which is yellowish and contains the albuminoid materials of the serum, while the upper part appears as an almost colourless transparent fluid. This contains little protein material and is as little toxic for anaphylactic animals as the whole serum. Moreover, it possesses antitoxic properties in very high degree. Hence the conclusion that the greatest part of the antitoxin contained in the total serum must have passed into the upper layer of the watery emulsion. In fact the thick sediment, containing the solid parts of the serum, no longer shows, when used alone, any antitoxic properties.

Experiments were especially made with antidiphtheritic and antitetanic sera, and it was found that both, if treated and made into an emulsion as stated above, gave an upper fluid part which protected sensitized animals against diphtheria or tetanus. In other words, Besredka appears to have discovered a means by which sera, without being deprived of their antitoxic properties, can be purified of the part to which anaphylactic shock is apparently due. It is for the clinician now to say whether these purified sera can be employed with advantage in practice. C. d. F.

Reynolds, F. E. On the results obtained by the Weil-Felix reaction for typhus fever at the garrison of Baku during the period March-July 1919 inclusive. *J. Roy. Army Med. Corps*, 1920, **35**, 25.

The author examined 73 persons by the Weil-Felix reaction for typhus; of these 32 were acute cases of typhus, 20 were convalescent, and the remainder suffered from other diseases.

Normal serum never gave a positive reaction in a dilution 1 in 50, but 1 in 100 was taken as a positive reaction.

Up to the eighth day of the disease one-third of the cases of typhus were positive and after this period all cases tested were positive. With regard to convalescents, up to the 30th day all were positive, but later cases were sometimes negative. The control cases with other diseases did not give reactions in a dilution of 1 in 100.

An agglutination of B. 'X 19' by a serum diluted 1 in 100 or more is thus diagnostic of typhus. P. F.

Golgi, C. Sulla struttura dei globuli rossi dell' uomo e di altri animali. **[On the structure of the red blood corpuscles of man and other animals.]** *Haematologica*, 1920, **1**, 1–15.

This quite original communication of Golgi was first published in the *Boll. d. Soc. med.-chir. di Pavia* (1919, **31**, 197), and deals with investigations carried out by means of the following two new methods: (1) Blood-films are fixed for 24–48 hours in equal parts of saturated solutions of mercury chloride and potassium bichromate. They are then transferred into equal parts of 2 per cent. mercury chloride and potassium bichromate to which 5–10 c.c. of 1 per cent. gold chloride and 5–10 drops of acetic acid are added. The films are observed in glycerol, starting from the second or third day after the last treatment until the fifteenth or twentieth day. (2) Drops of blood are fixed in a watch-glass by means of a fluid composed of 2 per cent. mercury chloride 60 c.c., saturated solution of picric acid 20 c.c., 1 per cent. osmic acid 10 c.c., acetic acid 5 drops, with the addition either immediately or after 8–24 hours of 10 c c. of 1 per cent. gold chloride for every 50 c.c. of fixative. Preparations are made from the sediment with some glycerol, from the second until about the tenth day after fixation.

Both methods show within the red blood corpuscles a peculiar body with a diameter of about one-third that of adult corpuscles and of about half that of foetal ones. This body occupies the central part of the erythrocytes, and, as demonstrated particularly by means of the second process, it appears to have a fine, sometimes more fibrillar, sometimes more reticular structure. Its contours, though clearly defined, are irregular, and there is no indication whatever of a limiting membrane. This 'reticulo-fibrillar apparatus' is not a nucleus, as the latter remains colourless by the new methods not only in the white but also in the nucleated red corpuscles, in which the apparatus appears concentrically arranged round the unstained nucleus. According to Golgi this apparatus does not correspond to any of the structures already described within the red corpuscles, but it reminds one a little of the endoglobular body recently demonstrated by Petrone by means of a lead impregnation method, which is not to be confused with the well-known bodies of Petrone. Golgi is convinced that the images obtainable by his two new methods are the expression of a real structure situated within the red blood corpuscles, but he does not feel able at present to express any opinion about their significance. The new methods stain also the centrosome in the white corpuscles of the circulating blood. C. d. F.

Gram, H. C. On the platelet count and bleeding time in diseases of the blood. *Arch. Int. Med.*, 1920, **25**, 325.

The author begins with a summary of the chief facts known with regard to blood-platelets. As regards counting them, he divides all methods in use into two groups:

1. Direct count—in dilutions after the ordinary haemocytometric principle, but using special liquids (Hayem, Afanassiew, Wright, Kinnicutt, &c.).
2. Indirect count—the relation of platelets to erythrocytes being counted in a variable dilution with a fixing liquid (Kemp, Brodie and Russell, Pratt, Fonio, &c.). This avoids the use of pipettes.

Then follows a brief outline of the technique of Oluf Thomsen. (See *Medical Science*, 1920, **2**, 582.) This method is adopted and elaborated. It is applied to several interesting groups of cases: normal platelet counts, 4 cases of haemophilia, a case of icterus haemolyticus, 14 of pernicious anaemia, 2 of aplastic anaemia, 5 cases of myeloid leukaemia, and 7 of lymphatic leukaemia.

The author considers that Thomsen's method gives reliable results. At the same time it permits of a determination of the prothrombin time by a slight alteration of Howell's technique, also a determination of the fibrin percentage according to an unpublished method elaborated by the author. The average number of platelets in normal individuals lies between 200,000 and 500,000 per c.mm. The platelets are diminished in number in pernicious anaemia, in most cases of lymphatic leukaemia, and in some cases of myeloid leukaemia. Normal values are found in haemophilia and augmented values in many cases of simple anaemia, and some of myeloid leukaemia. It is shown that platelet counts of less than 100,000 per c.mm. generally cause a tendency to bleed. The platelet count and bleeding time is important as a pre-operative measure, to differentiate, for example, aplastic anaemia from suspected occult cancer.

Note.—With reference to the formula employed by O. Thomsen in his method of counting platelets we pointed out (*Medical Science*, 1920, **2**, 583), in a review of his paper, that it was incorrect as printed. In a review of H. C. Gram's first paper (*Medical Science*, 1920, **2**, 583) Gram's formula, which is a modification of that of Thomsen, likewise contained an error. The corrected formula should be $Ps = Pp\ (Vsc - Vg)\,/\,Vsc - Vc$, with which Dr. Gram, from a personal communication, is in agreement. In the paper now abstracted (*vide* above) there is an error of translation whereby the Danish minus sign is represented by the English division sign. The final corrected formula for the important numerical investigation of platelets is

$$\text{Platelet count} = \frac{(\text{citrated blood} - \text{precipitate}) \times \text{platelets per c.mm. citrated plasma}}{\text{citrated blood} - \text{citrate}}$$

W. A. M. S.

Harvey, W. F. Estimation of erythrocyte and haemoglobin content of blood. *Indian J. M. Research*, 1920, **7**, 479.

This paper is divided into three parts:

I. Estimation of the volume of the erythrocytes. The method used is a variation of that described many years ago by Sir Almroth Wright. Comparison is made with a known normal blood under the same conditions of test. Minute details are given of the technique employed, the apparatus being quite simple. Three methods are described, viz. centrifugalization of whole blood, citrated blood, and settlement by gravity of citrated blood. Each method is criticized, citrated centrifugalized blood being the favourite. Then follows details of the way to calibrate the pipettes by mercury. Centrifuging is continued till the erythrocytes come to occupy a constant volume. The volume of the erythrocytes is calculated as a percentage of the total volume of blood used.

$$\text{Per cent. vol. erythrocytes} = \frac{\text{Height of column of erythrocytes}}{\text{Height of column of whole blood}} \times 100.$$

Degree of deviation from the normal is calculated as

per cent. vol. erythrocytes / per cent. vol. erythrocytes of normal blood.

II. Estimation of blood-content by tint and turbidity. To preserve blood indefinitely from haemolysis the author uses 10 per cent. formalin in 0·85 per cent. sterile salt solution. To preserve the tint of the blood hydrochloric acid was the only reagent tried and it did not prove satisfactory. The author here applies his tinturometer (described in *Indian J. M. Research*, 1917, **7**, 346) for the purpose of taking comparative readings.

III. Estimation of haemoglobin. The principle here used is that of Sahli's haemoglobinometer, with the alteration that the comparison is made with a descending series of successive dilutions of erythrocytes from a normal individual. A stock standard 1 per cent. solution is prepared by freeing the haemoglobin from 1 volume of blood with 9 volumes of N/10 HCl, then diluting this 10-fold with N/10 HCl. It is also pointed out that the tinturometer can be satisfactorily used as a haemoglobinometer.

Unfortunately, the author gives no figures of any application of the above three estimations to cases of disease. W. A. M. S.

Cramer, W. On glandular adipose tissue and its relation to other endocrine organs and to the vitamine problem. *Brit. J. Exper. Path.*, 1920, **1**, 184.

In all types of mammals investigated there exists a glandular type of adipose tissue histogenetically distinct from ordinary adipose tissue. It has been described under various names—'brown fat', &c. It has in all embryos a characteristic gland-like structure, and this structure is retained in some adults (hibernating animals, &c.). In most species it acquires the appearance of ordinary adipose tissue soon after birth. This tissue, which is very vascular, is functionally distinct from ordinary adipose tissue. Its fatty material is rich in cholesterin compounds and other lipoids in addition to true fat. This load of lipoids is retained under conditions which determine the disappearance of ordinary adipose tissue. 'Brown fat' is functionally related to the thyroid and adrenal glands. A close relationship exists between its lipoids and those of the adrenal cortex. The significance of the changes of the lipoids in the adrenal cortex is discussed and the interdependence of the cortex and medulla for normal functioning. If vitamines are completely withheld the lipoids disappear from the adrenal cortex and from the glandular adipose tissue, but this persists as a tissue and appears as a very vascular endocrine organ. Disturbance of the functional activity of this tissue will have to be considered in connexion with deficiency diseases. It is proposed to call it the 'lipoid gland' or the 'cholesterin gland'. P. F.

VIALE, G. Rapporti tra la temperatura dell' aria espirata e la temperatura cutanea. [**On the relation between the temperature of the expired air and the temperature of the skin.**] *Arch. per le sc. med.*, 1920, **43**, 40.

The investigations of Galeotti and his collaborators (Azzi, Barkan, Scaffidi) on the amount of H_2O given off in the breath and on the temperature of the expired air have led the way to the study of a question of great theoretical importance, both from physiological and pathological points of view. Galeotti's investigations were carried out at first by measuring by weight the quantity of aqueous vapour contained in a litre of expired air; but it very soon became evident that this datum was in direct relation with the temperature of the expired air, and research was therefore directed to the measurement of this temperature. Many experiments were then made by means of a very simple apparatus both in animals and man, and under various conditions. The results led Galeotti to put forward the following principles: (1) That the temperature of the expired air depends upon the vasomotor conditions of the lungs. (2) That there is a strict and direct relation between cutaneous and pulmonary vasomotor conditions in so far as pulmonary vasodilatation or vasoconstriction constantly follow the same cutaneous phenomenon.

The recent investigations of Viale were made in order to prove once more the truth of the above-mentioned principles. This time experiments were carried out in the Scientific Laboratories A. Mosso on Monte Rosa, because of the relative ease with which on high mountains, by simply exposing the subjects of investigation first to sun and then to shade, or vice versa, alterations are obtained in the vasomotor conditions of the skin. The changes in temperature of both the skin and the expired air in various conditions were carefully measured by means of a very sensitive galvanometer of the d'Arsonval type. The results obtained entirely confirmed Galeotti's theory that a strict relation exists between vasomotor conditions of the skin and temperature of the expired air in the sense that this temperature is constantly raised or lowered in accordance with a raising or lowering of that of the skin.

These experiments made on human subjects are interesting because of the light they throw on the pathogenesis of certain affections of the respiratory organs after sudden coolings of the surface of the body. They might also explain the mechanism of heliotherapy in pulmonary tuberculosis in so far as the cutaneous vasodilatation due to exposure to sunlight probably causes a corresponding pulmonary vasodilatation certainly useful for regenerative and cicatricial processes. A similar explanation might be given of the vasoconstrictor effect on pulmonary blood-vessels in haemoptysis of ice-bags applied to distant parts of the skin, as, for instance, that of the external genitalia. C. d. F.

NOVARO, P. (1). Ricerche calorimetriche comparative sul digiuno e sull' avitaminosi. Nota I. Del digiuno. [**Calorimetric investigations on inanition and deficiency disease. Note I. On inanition.**] *Pathologica*, 1920, **12**, 87.

Novaro, P. (2). Ricerche calorimetriche comparative sul digiuno e sull' avitaminosi. Nota II. Dell' avitaminosi. [**Calorimetric investigations on inanition and deficiency disease. Note II. On deficiency disease.**] *Pathologica,* 1920, **12**, 133.

Experiments were made on pigeons of known age submitted alternatively, though at different times, to inanition and then to a diet deficient in water-soluble accessory substance B, or vice versa. The results arrived at are: (1) In pigeons kept on a diet of polished rice the weight, body-temperature, and amount of heat given off do not show any alteration during a first period of 7–13 days. (2) After this time the amount of heat given off begins to diminish, the quantity of food taken is smaller, and the body-weight decreases. The temperature remains practically unchanged for a little while longer, and for another considerable period it is only one or two degrees Centigrade lower than the average normal temperature. In the last few days of the experiment, however, there is generally a lowering of even six degrees Centigrade. (3) Three to four days after it has begun to diminish, the amount of heat given off averages only 40 to 50 per cent. of the normal amount. (4) The loss in body-weight is greater when animals take less food. But this is comparatively still greater in animals kept on a diet deficient in accessory substance than in those submitted to starvation only, during which the diminution of body-weight is in direct relation to the amount of heat given off and to the length of the starvation period. (5) After the initial period, the temperature also is comparatively lower, and the amount of heat given off smaller in animals undergoing deficiency disease than in those merely starved. (6) In the last period of deficiency disease the amount of heat given off remains constantly small, whereas it increases in the corresponding period of starvation. The remarkable lowering of the body temperature without a corresponding increase of the heat given off in deficiency disease proves, according to the author, that in the latter the mechanism itself of heat production must be affected. (7) As soon as the animals experimented upon receive the vitamine of which they were deprived there is an increase in the amount of heat given off and in the body temperature. The body-weight, however, may continue to diminish unless the animals receive an unlimited supply of food. C. d. F.

Portier, P. Régénération du testicule chez le pigeon carencé. [**Regeneration of testis in pigeons deprived of accessory food substances.**] *Compt. rend. Acad. d. sc.,* 1920, **170**, 1339–41.

Partial removal of one testis was carried out in pigeons fed on sterilized polished rice; in other pigeons two operations of the same sort were performed, one before and the other during the period in which they were deprived of the water-soluble accessory food substance. When unmistakable symptoms of deficiency disease had appeared the animals were given food rich in vitamines and kept on such a diet for about three months. At the end of this period the pigeons were killed and both testes examined histologically. The author found that the testis operated upon was sometimes the same size, sometimes larger than the untouched one. This was generally of normal size. Histologically the partly regenerated organ had a normal structure and showed many signs of greater activity than the other one—a fact rather surprising, because the experiments were made in winter, viz. during the seasonal involution of normal testes in pigeons. For this reason the author puts forward the suggestion that the succession of states due to deficiency disease and normal nutrition ('revitaminization') plays an important part in the phenomenon described. C. d. F.

Bruno, G. L'intima struttura delle fibre del miocardio nell' ipertrofia cardiaca. [**On the minute structure of cardiac muscle-fibres in hypertrophy of the heart.**] *Arch. per le sc. med.*, 1920, **43**, 50–61.

Painstaking investigations were carried out in order to throw some light on the still obscure question of the structural changes which form the essential basis of myocardial hypertrophy. According to Bruno, this consists of an increase in the amount of contractile substance, in so far as the careful counting of myofibrils shows that their number is greater in the hypertrophic than in the normal myocardium. One cannot, however, exclude the suggestion made by other authors—that in myocardial hypertrophy the apparent units generally spoken of as myofibrils are larger than normally. As to the mechanism of the numerical increase of myofibrils, it appears to be similar to, if not identical with, that to which the post-embryonic development of the heart muscle-fibres is due, viz. longitudinal splitting of the myofibrils.
C. d. F.

Polettini, B. Sulle alterazioni delle pareti vascolari prodotte dall'adrenalina sia per iniezione in circolo, sia per contatto. [**On lesions of the vessel-walls caused by adrenalin.**] *Arch. per le sc. med.*, 1920, **43**, 63.

Repeated intravenous or intraperitoneal injections of fractional doses of adrenalin, constantly cause, in rabbits, aortic changes consisting of degeneration and necrosis of the plain muscle-fibres of the middle coat. These lesions are followed by distension, atrophy, fragmentation, and destruction of the elastic fibres. The degenerated places in the aorta become lastly extensively calcified. These alterations are identical with those found in the aortae of rabbits, the subjects of idiopathic arteriosclerosis; hence the conclusion that the arteriosclerosis of rabbits can be experimentally reproduced.

If adrenalin is directly applied to the walls of arteries, such as the carotid or the femoral, lesions can be observed which do not essentially differ from those caused by injections of adrenalin. But if adrenalin is directly injected into the urinary bladder no lesions of the plain muscle-fibres are produced, but only haemorrhages per diapedesin from the blood-vessels of the submucosa. These facts suggest the conclusion that the arteriosclerotic changes caused by adrenalin are very likely due to a local and direct influence exercised on the muscle-fibres of the arterial walls and only in part or very little to the hypertension which follows the passage of adrenalin into the blood-stream. How it is that the influence of adrenalin is felt by the muscle-fibres of blood-vessels and not by those of the wall of the bladder remains as obscure as the selective action of certain drugs and other substances on determined cells or tissues. C. d. F.

Cavara, V. L'epitelioma primitivo delle ghiandole di Meibomio. [**On primary epithelioma of the Meibomian glands.**] *Arch. per le sc. med.*, 1920, **43**, 1–39.

While carcinomata of the eyelids have been made the object of many observations, very little attention seems to have been paid to primary cancer of the Meibomian glands. Cavara, after a thorough search of the literature, has been able to trace the description, in most cases incomplete and not quite reliable, of fifteen adenomata and twenty-one carcinomata. All the data concerning them are by him very practically summarized in tabular form. He then gives an accurate description of a new case, and outlines, in the last part of his paper, the nosography of the disease, basing his conclusions both on his personal observations and on those of previous authors. From an histopathological point of view the malignant tumours of the Meibomian glands are non-keratinizing carcinomata showing a tendency to an alveolar arrangement. The epithelial masses lie primarily in the substance of the tarsus and are formed by large nodules of epithelial cells in the central part of which a cavity can frequently be recognized. This is due to degenerative changes of the cells which remind one to a certain extent of the normal metamorphoses of Meibomian cells. Here and there, but particularly in the peripheral parts of the tumour, smaller and more solid nodules of epithelial cells can be seen. The neoplastic cells are generally large, polygonal, and closely approximated to each other. Their nuclei are well stainable and their cytoplasm very often vacuolized. Though atypical, they have a remarkable resemblance to normal cells of the Meibomian glands. The connective tissue between the epithelial nodules shows generally a small-celled infiltration, particularly in the peripheral regions and near to the conjunctiva; the thinnest septa frequently show hyaline degeneration. The distinction between carcinoma and adenoma may be very difficult and almost impossible at the beginning of the disease. Epitheliomata of the Meibomian glands are not very malignant, and their progress can generally be stopped by timely and complete surgical intervention. C. d. F.

Russell, B. R. G., and Gye, W. E. The oxygen consumption of normal and cancerous mouse tissues *in vitro*. *Brit. J. Exper. Path.*, 1920, **1**, 175.

This paper contains an account of an investigation of the oxygen absorption of normal and malignant mouse tissues. The method of estimating the oxygen requirement of tissues has consisted chiefly in suspending the finely-minced tissue in defibrinated rabbit-blood, incubating at 37·5° C., and determining the oxygen content of the blood with a Barcroft differential blood-gas manometer. In two experiments mouse-blood has been used.

Of the normal tissues kidney is found to consume most oxygen, testis and embryo least. It would appear from the figures obtained for the different normal tissues tested that function is continued for a time after the tissues have been minced.

Malignant cells take up approximately the same amount of oxygen as the corresponding normal tissue cells. It is tentatively concluded that the oxygen consumption of malignant cells rises with increasing speed of growth, and further, that more oxygen is used by tumours which are more highly differentiated histologically. P. F.

Salazar, A. L. Sur la période chromatolytique de la granulosa atrésique de la lapine. [**The chromatolytic stage of the atresic membrana granulosa of the rabbit.**] *Mém. Soc. portugaise d. sc. nat., Série biol.*, 1919, **2**, 1–71.

As a result of the conditions leading to or accompanying ovulation the membrana granulosa of all large and medium Graafian follicles undergoes a peculiar, generally rapid, process of physiological involution in consequence of which the granulosa with or without the ovum becomes dissolved and connective tissue grows into the follicular cavity. This process, generally spoken of as atresia of follicles, has been the object of investigations which have been particularly concerned with the ovum, but not sufficiently with the atresic phenomena presented by the granulosa itself. These can be subdivided into three principal groups or stages, spoken of as pre-chromatolytic, chromatolytic, and post-chromatolytic, the term 'chromatolysis' being used to designate any metamorphosis shown by the nuclei of a variable number of cells of the granulosa during its involution. Salazar's paper deals principally with the chromatolytic stage. This is essentially characterized by the presence of peculiar, if not abnormal, mitotic figures, which do not lead, however, to the production of daughter-cells, but, through a process of coalescence of their chromosomes, to the formation of irregular bodies readily stainable by iron-haematoxylin. These are the 'siderophil' bodies, the process leading to their formation being termed the 'sideration'. The 'sideration' may take place at any of the mitotic phases, and the resulting bodies consequently show a remarkable polymorphism. And as the 'sideration' is accompanied by certain changes in the cell-protoplasm, the whole process results in the production of peculiar elements formed by an acidophil, round or ovoid, 'plasmodial mass' containing a variable number of bodies different in form and distribution. The plasmodial masses and their contents are the author's 'transitional forms', the process through which they are produced from the beginning of the mitosis being termed 'indirect chromatolysis'. The plasmodial masses, through further changes, give origin to smaller more stable forms ('formes d'equilibre') or 'chromocytes'. These are roundish corpuscles formed by an acidophil plasmatic part and by one or more chromatic basophil portions which, though variable in shape, have frequently a roundish or crescentic aspect with a hyaline sphere attached to them. Both the chromatic portions and the hyaline sphere are the product of the transformation of the siderophil bodies.

Chromocytes are produced not only through the predominant process of 'indirect chromatolysis' but also through common phenomena of nuclear pycnosis and caryorrhexis, as well as through the special forms of 'margination chromatolysis' and 'concentric chromatolysis', all of which play, according to Salazar, a secondary rôle in the chromatolytic stage of the atresic granulosa, and are collectively designated as the 'direct chromatolysis', no mitosis initiating their evolution. The chromocytes, however produced, undergo a progressive dissolution approximately coinciding with changes supervening also in the cells of the granulosa which have remained in a sort of quiescent state during the chromatolytic metamorphosis of the others. At that moment the chromatolytic stage ends and the post-chromatolytic begins.

In the last chapter of this interesting work, Salazar points out that phenomena similar to the 'indirect chromatolysis' have been observed in ova when also undergoing a process of involution and final dissolution, and he then comes to the conclusion that the atresia of the granulosa and that of the ovum, viz. of whole Graafian follicles, must have a common cause. In his opinion, this consists in a sort of hereditary decay of the mitosis, which, instead of being productive of new elements, leads to their involution and destruction. In this respect it is interesting to remember that processes analogous to the 'indirect chromatolysis' have been observed in endocrine glands and in the pancreas, and that the chromatin of the first polar body in rodents also passes through phases similar to, if not identical with, the 'chromatolytic' changes of the cells of the granulosa. Hence the more general suggestion that karyokinesis, to which we are in the habit of attributing a constructive significance only, may in given circumstances have also a destructive function. C. d. F.

Ladreyt, F. Sur le polymorphisme histologique de certains néoplasmes épithéliaux et les relations des néoformations inflammatoires et des tumeurs cancéreuses. [**Histological polymorphism of certain epithelial tumours; relation between granulomata and malignant new growths.**] *Comptes rend. Acad. d. sc.*, 1920, **170**, 1529–31.

From the histopathological examination of adenomatous polypi of the rectum, in which in some situations a cancerous transformation could be noticed, the author draws the following conclusions: (1) Inflammatory processes and tumours seem not to form two distinct groups but an unbroken succession. (2) The cancerous transformation is not a complication but a stage in the evolution of the disease. (3) Benign and malignant new growths are not different pathological entities but divergent evolutionary forms of the same lesion. C. d. F.

BIOCHEMISTRY

Almy, L. H., and **Robinson, R. K.** **Toxic action of ingested linseed meal on trout.** *J. Biol. Chem.*, 1920, **43**, 97.

At a commercial hatchery for trout in Rhode Island, a disease appeared in which many of the fish turned black, became blind, and showed curious nervous symptoms. A careful search for the cause of this revealed the fact that it was due to prussic acid poisoning caused by the eating of linseed meal. A glucoside present in the meal becomes split up and hydrocyanic acid is liberated. Linseed meal is apparently not usually toxic when taken into the stomach, because in the preparation of the meal the seed is submitted to a high temperature at which the enzyme causing splitting of the glucoside is destroyed. R. A. P.

Mansfeld, G. Beiträge zur Physiologie der Schilddrüse. IX. (Zur Abwehr.) [**Contributions to the physiology of the thyroids. IX. (In defence.)**] *Arch. f. d. ges. Physiol.*, 1920, **181**, 249.

Polemic with Hári. The author reasserts that the increased nitrogenous metabolism after oxygen lack is due to excessive action of the thyroids; that chloroform administration does not increase the nitrogenous metabolism in thyroidectomized animals as it does in normal animals; that after thyroidectomy there is no augmentation of nitrogenous metabolism following the establishment of a febrile state, e.g. by injection of *B. coli*. The relation between the thyroid and blood-formation is also discussed: arsenic was ineffectual in thyroidectomized animals, while iron had its usual effects. C. L. E.

Eckstein, A. Die Totenstarre des Herzens. [**Rigor mortis of the heart.**] *Arch. f. d. ges. Physiol.*, 1920, **181**, 184.

The author concludes, with Volkhardt and others, that the condition of the heart at autopsy is no indication of its state at the time of death. The present series of experiments, made on hearts of cold-blooded animals and mammalia, showed that in the course of death the heart first underwent a dilatation and then a contraction: the latter may be either continuous, or may take place in a series of steps, each of which corresponds to a spontaneous contraction followed by incomplete recovery. Cardiac muscle is capable of responding to stimuli until quite dead, but in the later stages of the survival is prone to enter into immediate rigor when stimulated. The condition of different parts of the same heart may be different during the onset of rigor. C. L. E.

Walter, H. Beiträge zur vergleichenden Physiologie der Verdauung. VIII. Das Verhalten der Hefezellen gegen Proteasen. [**Contributions to the comparative physiology of digestion. VIII. The behaviour of yeast cells towards proteases.**] *Arch. f. d. ges. Physiol.*, 1920, **181**, 271.

Microchemical and chemical observations on yeast digested *in vitro* agree with the results of the metabolism experiments of other investigators in indicating a high degree of availability of the yeast proteins, when the yeast is subjected to peptic or pancreatic digestion. This does not, however, appear to apply to the fats to the same extent. C. L. E.

Kahn, R. H. Zum Problem des Herzalternans. [**The problem of alternation of the heart.**] *Arch. f. d. ges. Physiol.*, 1920, **181**, 65.

Straub's explanation that alternation is due to a prolonged contraction with a high frequency, so that the second smaller contraction starts from a higher diastolic intraventricular pressure than the preceding larger systole, is shown not to fit all the facts. Thus it does not hold good for the heart alternation seen in dogs to which glyoxylic acid has been administered, since in these hearts the smaller contraction starts from the more relaxed ventricle. The author's view is that in alternation both the large and the small beats are abnormal, and this view is supported by the study of heart-sounds and electrocardiograms; the first heart-sound is shorter than normal, and the systole, particularly in the large beat, is prolonged. The explanation is to be sought in altered properties of the cardiac musculature. C. L. E.

Linzenmeier, G. Untersuchungen über die Senkungsgeschwindigkeit der roten Blutkörperchen. I. Beobachtungen am menschlichen Blut. [**Investigations on the velocity of sedimentation of blood corpuscles. I. Observations on human blood.**] *Arch. f. d. ges. Physiol.*, 1920, **181**, 169.

The accelerated sedimentation and agglutination of the corpuscles which is seen in the blood during pregnancy is due to the removal of the negative electric charge of normal corpuscles by a (positively charged) substance present in the plasma. If the blood-plasma be treated with substances such as animal charcoal or kaolin, which adsorb positively charged particles, the rate of sedimentation of the corpuscles is retarded, while shaking with the hydroxides of Fe, Al, or Ce, which have the reverse effect of removing negatively charged colloids, leaves the rate of sedimentation unchanged, or may even accelerate it. The sedimentation of the corpuscles is also delayed by removal of fibrinogen, by narcotics, or by previously heating the plasma, while the addition of gelatin or gum arabic accelerates the deposition. C. L. E.

Borčić, B. Ein Beitrag zur Frage der antigenen Wirkung der Bakterienfette. [**A contribution to the question of the antigenic effect of bacterial fats.**] *Biochem. Ztschr.*, 1920, **106**, 212.

The author has not been able to get antigenic effects with bacterial fats. Fats from the following bacteria have been tried: typhoid, diphtheria, cholera, and *Staphylococcus*. The treatment of rabbits with the excreted fat practically never produced any agglutination effect upon serum. This does not support the opinions of Stuber and Bauet. The fatty bodies also show no antigenic effects when injected into the animal body. R. A. P.

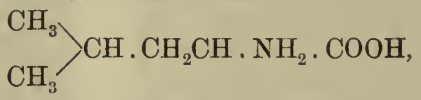
Lewis, H. B., and Root, L. E. Amino-acid synthesis in the animal organism. Can normal leucin replace lysin for the nutritive requirements of the white rat? *J. Biol. Chem.*, 1920, **43**, 79.

The question as to whether the animal body is able to make for itself any of the essential amino-acids is clearly one of considerable importance. In certain perfusion experiments upon the surviving liver, it has been shown that several of the amino-acids can be made from the corresponding hydroxy-acids. The body substitutes an NH_2 group for the OH group. Hopkins and Ackroyd have shown that the amino-acids, arginin, and histidin can replace one another at any rate in part. The question is really a fundamental one in protein metabolism, as protein molecules are made up of amino-acids, and the degree to which synthesis is possible determines how far we are dependent upon our diet.

In the paper by these authors an attempt has been made to see whether the essential amino-acid lysin

$$CH_2.NH_2-CH_2.CH_2.CH_2.CHNH_2.COOH$$

can be replaced in a diet by normal leucin,



$$\begin{matrix}CH_3\\ CH_3\end{matrix}\!\!>CH.CH_2CH.NH_2.COOH,$$

the argument being that a replacement of lysin by leucin would indicate a power of making the amino substitution. Rats fed upon a diet deficient in lysin would not grow when leucin was added. The results of the work were therefore negative. R. A. P.

Pelkan, K. F. Relation of urochrome to the protein of the diet. *J. Biol. Chem.*, 1920, **43**, 237.

The question of the significance of the urochrome pigment in the urine has never been settled satisfactorily. Garrod held the view that it was derived from the urobilin, while others have thought that it came from the blood. Pelkan found that a reduction of the protein intake decreased the amount of this pigment excreted. An addition of carrots to the diet, rich as they are in the plant yellow pigment, did not increase the excretion of urochrome. So it is apparently not carotin. Further work revealed the existence in both peptone and casein of a body corresponding in every way to urochrome. The presence of this body, correlated with the increase of urochrome on a high protein diet, suggests that urochrome is in large part derived from the protein of the food. R. A. P.

Haggard, H. W., and **Henderson, Yandell; and the latter author alone. Haemato-respiratory functions. III. The fallacy of asphyxial acidosis. IV. How oxygen deficiency lowers the blood-alkali. V. Relation of oxygen tension and blood-alkali in acclimatization to altitude.** *J. Biol. Chem.*, 1920, **43**, 3.

The current view at the present time is that the increased breathing produced by deficiency of oxygen is due to the appearance of acids such as lactic acid in the blood, followed by a decrease in the amount of blood-alkali. That this is not the whole story is the result of some experiments given by these authors. In these experiments it was shown that as a response to diminished oxygen an increase of breathing will occur a perceptible time before the neutralization of blood-alkali. The discrepancy seems to be due to the fact that while stress has been laid upon the temporary increase of acid reaction due to the appearance of temporary increase of CO_2 pressure in the blood, no account has been taken of the subsequent effects. These are considered here to be the blowing off of CO_2, and then, in the attempt of the body to adjust itself to the lowered blood-alkali, the disappearance of alkali from the blood. This leaves the body with less alkali for carrying round the CO_2, and so there is a need for increased respiration. The effect is really an alkalosis. In other words, in addition to the acidotic process, we have also to take into account this acapnial process, followed by the subsequent alkalosis. R. A. P.

Rother, J. Beiträge zum Nukleinstoffwechsel-Problem. Über Harnsäureausscheidung nach parenteraler Zufuhr von Purin-Nukleosiden beim gesunden Menschen. [**Purin metabolism. Uric acid excretion after parenteral administration.**] *Ztschr. f. physiol. Chem.*, 1920, **110**, 245.

Thannhauser, one of whose papers is reviewed in this number, believes that the purins circulate in the blood as complexes in the form of nucleosides or nucleotides. In healthy individuals the uric acid is excreted as soon as it is released from these complexes. In gout, the uric acid is retained in consequence of failure of the kidney or some other mechanism to eliminate it. Rother introduced the nucleosides, guanosin and adenosin, in 1·0 grm. amounts intramuscularly, and found that the uric acid excreted only 17·8. 78·8 per cent. of the uric acid calculated reappeared in the urine. He does not believe that the process of converting purin complexes to uric acid is a quantitative one. The patients, with the possible exception of one, were non-gouty in type. C. G. L. W.

Thannhauser, S. J., u. **Czoniczer, G.** Experimentelle Studien über den Nukleinstoffwechsel. IX. Über den Nachweis und die Bestimmung von gebundenen und freien Purinen im menschlichen Blut und Eiterserum. [**Purin metabolism. IX. The detection and estimation of free and combined purins in human blood and pus serum.**] *Ztschr. f. physiol. Chem.*, 1920, **110**, 307.

By the precipitation of the blood proteins—on the one hand by an acid uranium acetate solution and with salicylsulphonic acid on the other —under definite conditions, T. and C. have been able to obtain filtrates which contained only the free purins and those which contained the free purins together with those in combination as nucleotides. The purin content of the filtrates was determined by the Krüger-Schmid method. The uric acid method was estimated separately colorimetrically. From the table presented it is seen that in normal individuals the amount of nucleotide nitrogen per 100 c.c. of blood is 2–3 mg. The free purin nitrogen is 1·0–1·5 mg. If this latter be multiplied by 3, the result corresponds closely to the uric acid present in the blood, showing that very little free purin other than uric acid is present. The amount of nucleotide nitrogen is about twice that of the free purin nitrogen.

These experiments, done in quite another way, form a much desired confirmation of the results of Benedict (*J. Biol. Chem.*, 1915, **20**, 633), who observed a similar condition in ox blood. The definite detection of combined purins in the circulating blood adds a new factor in the study of the pathology of gout, and a further investigation may give us results of great value regarding this very obscure condition. T. and C. are publishing some information of this character in a current number of the *Deutsches Archiv. für klinische Medizin.* C. G. L. W.

Plimmer, R. H. A. Note on 'scurvy' in pigs. *Bio-Chem. J.*, 1920, **14**, 570.

Four young pigs showed the following symptoms: stoppage of growth; sensitiveness to touch; lack of appetite, and lassitude; spasmodic twitching of limb muscles; swollen joints; inability to walk or stand. They had been fed on a diet of cooked food composed of meal, sharps, and turnips. On adding raw turnip to the diet an immediate improvement was noted. In four weeks they were walking on straight limbs. The defect was due to an absence of the antiscorbutic factor in the diet due to destruction by heat.

C. G. L. W.

Jess, A. Die Monoaminosäuren der Linsenproteine. [**The amino-acids of the lens.**] *Ztschr. f. physiol. Chem.*, 1920, **110**, 266.

The author has been engaged for some years in a chemical investigation of the processes taking place in cataract. He has shown with Reiss that the cystin reaction is almost lacking in the cataract lens. It is also seen that in young lenses α- and β-crystalline—proteins soluble in water—make up the greater part of the lens. These gradually decrease in quantity with age, and with this decrease sclerosis and loss of accommodation occurs. This process is even more evident in cataract lenses. In order to investigate the specific qualities of the proteins of the lens, these were separated from 3,000 bullocks' eyes with α-crystalline, β-crystalline, and albumoid. It was shown that albumoid, the water-insoluble constituent, was poor in valin and alanin, while these two amino-acids are present in considerable quantity in α- and β-crystalline. C. G. L. W.

Bircher, Max Edwin. Die Beziehung zwischen der Viscosität des Blutes und dessen Gehalt an Blutkörperchen und gelöstem Eiweiss. [**The relation between the viscosity of the blood and its content of corpuscles and dissolved protein.**] *Arch. f. d. ges. Physiol.*, 1920, **182**, 1.

The viscosity depends principally on the number and volume of the corpuscles, and on the amount and nature of the dissolved colloids. The effect of alteration in the number of corpuscles per unit volume is not necessarily constant, since an important factor is the size of the corpuscles, and methods for determining the number of corpuscles from viscosimetric measurements are therefore unreliable.

As regards the volume of corpuscles, the results are less irregular and more nearly conform to the formula

$$\eta s = \frac{\eta}{I - K}$$

where $\eta s =$ the viscosity of the suspension (blood): $\eta =$ that of the plasma, and $K =$ the volume of corpuscles present.

The most accurate determination of the volume from viscosimetric data is obtained by the author's modification of Ulmer's method. The principle of this is that a measured volume of serum is drawn off from the centrifuged blood, an equal volume of saline solution is added to the residue, mixed, and again centrifuged and drawn off. From the viscosity at various dilutions of the pure and diluted sera the volume of serum in the original blood can be determined.

As regards the effect of proteins on the viscosity of the serum or plasma it was found that the viscosity is no regular index of the protein content, since this differs according to their nature. C. L. E.

Wiechmann, E. Zur Theorie der Magnesiumnarkose. [**The theory of magnesium narcosis.**] *Arch. f. d. ges. Physiol.*, 1920, **182**, 74.

The appellation 'magnesium narcosis' is unjustifiable, since the effect of Mg is on the synaptic tissues, and on automatic tissues such as the heart and alimentary canal. These effects can be antagonized by Ca, but Mg also has an effect on muscle which cannot be so neutralized. Mg can be replaced by Co, Ni, Mn, or by the complex hexaminocobaltichloride, and Ca can be similarly replaced by Sr or Ba as regards the antagonistic actions. The former group causes swelling of minced muscle, while the latter causes shrinkage. C. L. E.

Abderhalden, E. Weitere Beiträge zur Kenntniss von organischen Nahrungsstoffen mit spezifischer Wirkung. [**Further contributions to the knowledge of organic foodstuffs with specific action.**] *Arch. f. d. ges. Physiol.*, 1920, **182**, 133.

The effect of yeast in protecting pigeons fed on polished rice was investigated. Very small daily amounts of yeast (0·05 – 0·1 grm.) suffice, but, after such treatment, illness rapidly supervenes when the birds are transferred to pure rice. It is suggested that the deficiency factors are essential regulators of tissue metabolism, of the nature of co-ferments.

C. L. E.

Verzar, F., u. Gara, M. Beiträge zur Methodik der Blutgasanalyse. [**Methodological contributions to blood-gas analysis.**] *Arch. f. d. ges. Physiol.*, 1920, **183**, 235.

Modifications of the Barcroft technique for gaseous exchanges, &c. (1) For conservation of blood samples for some hours previous to analysis, 1 c.c. of the following solution is placed under 2 cm. of liquid paraffin in a test-tube: liq. ammon. fort. 2·0 c.c., Na citrate 5·0 grm., saponin 0·5 grm., water to 100 c.c. This haemolyses the sample of blood, which is accurately measured out into the solution without admission of air. Samples are then withdrawn for analysis. (2) A 6-way tap for the collection of successive samples of venous blood without altering the position of the vein cannula, &c.

C. L. E.

Abderhalden, E., u. **Gellhorn, E.** Studien über die von einzelnen Organen hervorgebrachten Stoffe mit spezifischer Wirkung. III. [**Studies on the substances with specific actions manufactured by certain organs. III.**] *Arch. f. d. ges. Physiol.*, 1920, **182**, 28.

Various endocrine organs were subjected to the action of pepsin-HCl, trypsin, and intestinal juice, and the hydrolysed products (or optones) examined for their action on the enucleated frog's eye and on the excised frog's heart. Optones from corpus luteum and testis were mydriatic and caused arrest of the heart in diastole; that from thymus also dilated the pupil, but had little effect on the heart. Hypophysis and thyroid-optones were myotics with little effect on the heart. The mydriatic action of adrenalin is augmented by optones from the ovary and anterior lobe of the hypophysis. With the exception of the combination thyroid-testis, which caused constriction of the pupil, the mydriatic effect was predominant in mixed optone solutions. It does not necessarily follow that substances having these physiological effects are present in the living glands.

C. L. E.

Rohde, K. Zur Physiologie der Aufnahme und Ausscheidung saurer und basischer Farbsalze durch die Nieren. [**The physiology of the intake and excretion of acid and basic dye-salts through the kidneys.**] *Arch. f. d. ges. Physiol.*, 1920, **182**, 114.

The investigation represents an experimental inquiry into conditions of intravitam staining. Experiments were made on frogs to which the dyes were administered by way of the blood or lymph-stream or by feeding. In some cases the reaction of the blood was changed by the administration of boric acid or sodium carbonate by the mouth, and the urine was collected and examined for reaction and for the presence of dyes. Basic dyes were more readily excreted when the blood (and presumably the tissues) had an alkaline reaction, while for acid dyes the reverse held good. In normal frogs basic dyes were more readily absorbed and excreted than acid dyes. All dyes which are not too highly colloidal can act as vital stains, provided the physico-chemical conditions are suitable. The size and arrangement of the cell-granula depend on the physiological condition of the cell; in resting cells the granula are small, and in actively working cells they are large. High colloidal basic dyes are more toxic than low colloidal ones for normal frogs; for alkaline frogs the former are more readily borne, while for acid frogs the latter are less supportable than for normal. The reverse holds good for high and low colloidal acid dyes. These results, while not in complete accordance with the lipoid-solubility theory of intravitam staining, lend still less support to the ultra-filtration view, since the dispersion of acid dyes is diminished by acids and that of basic dyes by alkalis, yet it is under these conditions that the dyes are taken up most readily by the cells. C. L. E.

Abderhalden, E., u. **Schiffmann, O.** Studien über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. IV. [**Studies on the substances with specific actions manufactured by certain organs. IV.**] *Arch. f. d. ges. Physiol.*, 1920, **183**, 197.

Feeding experiments with thyroid and various extracts of hydrolysed thyroid on tadpoles showed the usual effects on metamorphosis; changes in the intestines were studied histologically and shown to be accelerated. No effect could be demonstrated on the hypophysis, thyroid, or thymus of the tadpoles. C. L. E.

Drummond, J. C., and **Coward, K. H. Researches on the fat-soluble accessory substances. V. The nutritive value of animal and vegetable oils and fats considered in relation to their colour.** *Bio-Chem. J.*, 1920, **14**, 668.

The value of a fat as the source of fat-soluble A is not contingent on being of vegetable or animal origin. The animal oils are, as a class, superior to vegetable oils as growth-promoting factors. Palm oil approaches animal oil in this respect. Winter feeding of cows lowers the amount of growth factors in the butter produced. C. G. L. W.

Drummond, J. C., and **Coward, K. H. Researches on the fat-soluble accessory substances. III. Technique for carrying out feeding tests for vitamin A** (**fat-soluble A**). *Bio-Chem. J.*, 1920, **14**, 661.

Great care should be taken that the basal ration is as free as possible from the vitamine which is being investigated. Caseinogen is heated to 102° C. for 24 hours, and is then subjected to prolonged extraction with alcohol and ether. Rice starch in the crude form is almost entirely free from fat-soluble A. A fully hydrogenated cotton-seed oil is employed as the vitamine-free fat. C. G. L. W.

Drummond, J. C. The nomenclature of the so-called accessory food factors (vitamins). *Bio-Chem. J.*, 1920, **14**, 660.

It is suggested that the final ‘e’ be dropped in the word vitamine, and suffixes A, B, and C be used instead of fat-soluble A, &c. C. G. L. W.

Campbell, J. A. Ammonia excretion, amino-acid excretion, and the alkaline tide in Singapore. *Bio-Chem. J.*, 1920, **14**, 603.

It has been noted that the amounts of ammonia excreted by the natives of the Straits Settlements were high in comparison with European standards. An attempt is made by the author to determine whether the influence of climate and the method of taking meals would account for the difference. The hourly excretion of ammonia was determined to see if an alkaline tide exists. The largest daily amounts of ammonia were excreted by subjects exposed most to the hot moist climate. Well-marked alkaline tides were the rule three hours after any meal. C. G. L. W.

Homer, A. The heat inactivation of diphtheria antitoxin. *Bio-Chem. J.*, 1920, **14**, 565.

The addition of 1·5 to 2·0 per cent. of sodium chloride to plasma, whether non-cresylized or cresylized prior to its being heated, in no way reduces the extent of the heat inactivation of the antitoxin. The rôle of the heat inactivation of the antitoxin is a function of the temperature to which it is heated. With progressive rise in temperature the proportional loss of antitoxic value in a given time rapidly increases until at 72° C. there is a 60 per cent. inactivation of the antitoxin within ten minutes. The extent of the heat inactivation of the antitoxin in an aqueous solution of the antitoxin-bearing proteins is considerably less than that evidenced during the heating of antitoxic plasma. C. G. L. W.

Annett, H. E. Factors influencing alkaloidal content and yield of latex in the opium poppy (*Papaver somniferum*).

Annett gives in this article an interesting account of the method of harvesting opium, and the effect of methods on yield; experiments in heredity, manuring, &c., are detailed. He concludes that morphin is a useless end product of metabolism, and is stored in the capsule where it cannot harm the plant. C. G. L. W.

Maclean, H., and **Griffiths, W. J.** **Cuorin.** *Bio-Chem. J.*, 1920, **14**, 615.

The substance cuorin separated as a lipin substance from heart-muscle is a decomposition product of the tissues, the change taking place during extraction. The only phosphatides present in animal tissues are lecithin, kephalin, and sphingomyelin. C. G. L. W.

Biehler, W. Zur Methodik der Harnacidimetrie (insbesondere für klinische Zwecke). [**The clinical estimation of urinary acidity.**] *Ztschr. f. physiol. Chem.*, 1920, **110**, 298.

A special colorimeter with prisms filled with coloured gelatin is described. The method does not seem to possess any great advantage over those previously in use. C. G. L. W.

Coward, K. H., and **Drummond, J. C.** **Researches on the fat-soluble accessory substance. IV. Nuts as a source of vitamin A.** *Bio-Chem. J.*, 1920, **14**, 665.

Brazil, barcelona, pea, walnuts, almonds, and butter-nuts possess a relatively low food value as sources of vitamine A. The accessory is formed in the green part of the living plant, and is not stored to any appreciable extent as such in the seed and other resting tissues. C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radium Therapy.

Pfahler, G. E. **The treatment of recurrences and metastases from carcinoma of the breast by means of radium and Roentgen rays.** *Am. J. Roentgenol.*, 1920, **7**, 328.

The author describes the effects obtained by radium and by X-rays, and the respective advantages of these agents. A comparison is made at some length of the intensity at 10 cm. below the skin of hard X-rays and of γ-rays as obtained from radium in the amount and with the technique commonly employed. It is shown that the proportion of the surface dose which penetrates to a depth of 10 cm. is nearly five times greater in the case of X-rays than in that of γ-rays.

Hence the conclusion reached, that radium should be used for all palpable recurrent or metastatic nodules, especially in the operation scar, the axilla, and suprascapular regions, and X-rays for the general treatment of the carcinomatous area, and for mediastinal and pulmonary disease. Warning is given as to the use of both agents over the same skin area.

E. M. W.

Janeway, H. H. **The use of buried emanation in the treatment of malignant tumours.** *Am. J. Roentgenol.*, 1920, **7**, 325.

The author gives a brief summary of the indications for the use of buried emanation tubes in the treatment of malignant tumours in the mouth and fauces, rectum, cervix uteri, prostate, bladder, breast, lymphatic nodes, and sarcoma of the extremities. The advantages claimed for this method of treatment of growths of mucous membranes are accuracy of the primary application, economy in the use of radium, and ease of dealing with residual remnants of tumours.

The most practical guide to dosage is the area of the plane of the largest diameter of the tumour. A comparative table is given showing the dosage in millicuries required on this basis for circular, oval, and spherical tumours. E. M. W.

Discussion of Drs. Janeway's and Pfahler's articles at the fifth annual meeting of the American Radium Society. *Am. J. Roentgenol.*, 1920, **7**, 333.

Points emphasized in the discussion on the papers were:

(1) That if the radium used is distributed over the surface, giving a plaque effect, the effect on the skin is reduced and the deep effect obtained is comparable with that of X-radiations at 25 cm. skin-target distance.

(2) That very large amounts of radium used at a distance from the skin produce deep effects comparable with those of X-rays from a source at the same distance.

(3) That dosage by buried emanation in millicurie hours can be compared with that by radium needles in milligram hours, but to obtain the same effect with needles the dosage in milligram hours must be smaller than that in millicurie hours with tubes.

(4) That the constitutional effects of large doses of X-rays may usually be avoided by giving smaller daily doses (from two to four erythema doses) until the full dose required has been administered, instead of giving the complete dose at one sitting.

(5) That post-operative swelling of the arm may frequently be relieved by treatment with radium or X-rays. E. M. W.

Morson, Clifford. The rôle of radium in the treatment of malignant disease of the bladder and male genital organs. *Brit. J. Surg.*, 1920, **8**, 36.

Morson first discusses the rôle of radium in the treatment of malignant disease of the bladder; on general grounds he advises the introduction of the radium into the substance of the tumour, the growth having previously been irrigated with antiseptics twice daily for a week. As soon as the skin wound has healed, arrangements are made for permanently draining the bladder above the pubes: the device used consists of a curved metal tube which passes through a metal shield and fits on to a rubber tube which terminates in a rubber bag fixed to the inner side of the thigh by straps.

The author summarizes the principal changes which are observed as sequelae to adequate irradiation of the malignant mass: (1) Rapid degeneration of the malignant cells in the immediate vicinity of the tube of radium (2) Apparent vacuolation and enlargement of nuclei of those cells beyond the degeneration zone. (3) Loss of the reproductive function of the cancer-cell. (4) Proliferation of the connective tissue cells, which change shows a similarity to the attempt of nature to arrest the development of cancer through new formation of fibrous tissue. (5) Thrombosis of the blood-vessels, which leads to the arrest of haemorrhage and shrinkage of the malignant mass.

In cases of malignant disease of the prostate the author is again in favour of the insertion of the radium into the growth, the procedure advocated being as follows: the patient, under general anaesthesia, is placed in the lithotomy position. A sound is passed per urethram into the bladder, and an incision made along the median perineal raphé. The tissues between the anterior wall of the anal canal and membranous urethra are then separated. By inserting the finger into the space between the anal canal and membranous urethra the lower pole of the prostate is felt. With the finger as guide, the radium tube is passed into the substance of the gland between the urethra in front and the rectum behind. To obviate the necessity of using a knife, the tube should have one end pointed. Care must be taken that the radium is not pushed into the urethra; the presence of the metal sound should be of assistance in avoiding this error.

Regarding the indications for use of radium, the author considers that it is the method of choice only when the growth has infiltrated the surrounding tissues, e.g. the base of the bladder, the vesiculae seminales; surgical measures are advocated when the disease has not spread beyond the capsule of the prostate.

The author lays stress throughout the paper upon the injurious effects of the rays upon the normal tissues of the body as a result of too prolonged irradiation. S. R.

Nogier, T. Considérations sur le traitement par le radium et la technique d'application dans les néoplasmes au col et du corps utérin. [**Treatment by radium and the technique of application in neoplasms of the uterine cervix and body.**] *Paris méd.*, 1920, Feb. 7. (*Arch. d'électric. méd.*, 1920, **28**, 220.)

There are two principal factors to bear in mind: the dose of energy used, and the technique. The radium rays must act on the centre of the neoplasm. They must be filtered in a manner suitable to the shape and extension of the neoplasm. Application should be not to the vaginal culs-de-sac, but to the cervix or to the body of the uterus. If there is no passage, one must be made by moderate curettage or by dilatation. In this way the whole of the radium radiation is used. Everything possible must be done to make the case as nearly as possible of the ideal type, that of the spherical tumour, in which the radium is placed in the centre. Moreover, the rays must be suitably filtered. When tubes of condensed emanation are used, alpha- and beta-rays, which are not sufficiently penetrating, must be eliminated by metal sheath-filters of high atomic weight (silver, gold, platinum, or lead).

When tubes of radium are used, in which the salt is enclosed in a platinum covering, filtration is already effected, but this relative filtration is not always enough, as insufficient attention is usually paid to the most penetrating rays, whether they be X-rays or radium rays. When these radiations are suitably filtered, they have a selective action on the cells of the new growth. Alpha-rays destroy everything, healthy and diseased cells alike, and it is almost the same in the case of beta-rays. Many perforations are due to the injurious action of too abundant and insufficiently filtered rays. On the other hand, at the external wall of the platinum tubes, as of the sheath-filters, a secondary radiation is produced, resembling the alpha-ray in its feeble penetration. This must be eliminated by a covering of such thin material as paper, silk, cork, or gauze.

An almost isolated destructive action will be obtained by placing in the tumour tubes of condensed emanation contained in a thin metal sheath; a strong destructive action combined with a weak modifying action will be obtained by placing unscreened 0·5 mm. platinum tubes in the tumour; a powerful and progressive modifying action will be obtained by the previous inclusion of tubes of radium in the metal sheath-filters and by a second covering of paper, silk, or gauze to eliminate the secondary rays.

The rapidity with which the action takes place will naturally vary inversely with the amount of filtration. S. U. L.-B.

Radium Technique.

Failla, G. Radium technique at the Memorial Hospital, New York. *Arch. Radiol. & Electroth.*, 1920, **25**, 3.

The source of radiation used is either the emanation or the active deposit of radium, the former being sealed in small glass tubes of two sizes, the larger, 0·6 mm. in diameter and 10 to 15 mm. long, contain initially from 100 to 250 mc. of emanation, whilst the smaller, 0·3 mm. in diameter and 3 mm. long, contain from 1 to 4 mc. each. The stronger tubes are encased in enamelled silver tubes 0·5 mm. thick, and the strength of these and the bare tubes is measured by an ionization method. The manufacture of bare tubes demands considerable skill and long exposure to the radiation on the part of the technician, and for this reason the tubes are now machine made.

Besides the silver tube-filter, which, with its enamel, absorbs 90 per cent. of the radiation given off by the glass tubes, filters consisting of 1·5 to 1 mm. of platinum, 2 mm. of lead, 0·5 mm. of silver, 0·5 to 0·2 mm. of aluminium, rubber, wood, and paraffin are now used.

Dental compound applicators moulded to the particular lesion are used, deep grooves, filled with paraffin, in which lie embedded silver tubes of the requisite strength, traversing the area corresponding to that to be treated.

Many patients have been treated by inserting in the growth, by means of a steel trocar, tiny tubes containing preferably 1 to 2 mc. of emanation, and leaving them to decay *in situ*.

The author describes three types of X-ray applicators for deep radium therapy. One consists of a flat box, the bottom of which is lined with lead, holding many silver tubes, containing in all from 1,000 to 2,500 mc. of emanation; another is a dental compound mould, 2 to 4 cm. thick, to which is attached a lead tray containing the requisite number of tubes. The third is a block of wood lined with lead on all faces except one which is parallel to that covered with silver tubes, held in position by adhesive tape.

The special applicators described are those designed by Dr. H. Bailey for the treatment of uterine cases, and by Dr. Barringer for the treatment of cancer of the bladder.

Active deposit is used, either on lead foil for the treatment of vernal catarrh, or on common salt, which is then dissolved in distilled water, thereby giving a radio-active solution suitable for injection. The method of preparation of the active deposit is described in each case. L. H. C.

Baud, M., et **Mallet, L.** A propos de l'émanation comparée aux sels du radium. [**Radium emanation compared with radium salts.**] *Presse méd.*, 1920, February, 115. (*Arch. d'électric. méd.*, 1920, **28**, 221.)

Danne had recommended the use of radium emanation, and Regaud put this technique into practice at the Curie Institute. From numerous articles it appears that the medical world is of the following opinion:

(1) Emanation is essentially superior to salts of radium: 'the results are better when it is used'.

(2) Emanation alone 'permits of large doses', the usefulness of which is known in certain delicate or painful applications, and the excellent results of which are vaunted a little too soon.

(3) Emanation permits of 'a small price for application'; it will render radium therapy a 'cheap' treatment, 'available even for the poorest'.

Now, the use of salts of radium or of emanation in corresponding quantities gives an identical irradiation whose biological and therapeutic effects are the same. Large doses can be as easily obtained from salts of radium as from emanation. A gramme of radium which gives a curie of emanation when radio-active equilibrium is realized, that is to say, in rather exceptional cases, could be applied just as efficaciously in the form of salts of radium whose irradiation is constant, and for that reason is superior to emanation apparatus. Hence the use of emanation is not less expensive than use of radium salt; it is even more so in certain cases. The authors, however, in spite of these criticisms, do not detract from the practical interest of emanation used according to the technique of the American laboratories, in London, and in Manchester. They regret that there is no such organization in France. For this reason a better use of radium salts must be sought. Regaud complains of the cost, of the risks of loss and of deterioration (there is no ground for this criticism), that they are practically unchangeable, that they only lend themselves to an invariable technique, that they occupy a relatively considerable space, that they hinder a rational use of radio-active energy, and that they ultimately conduce to a certain waste of this energy. The authors admit these last three assertions, but they speak of the approaching completion of an apparatus which will assure utilization of radio-active energy with variations and diversities closely approaching those from the use of emanation.

S. U. L-B.

Electro-diagnosis.

Philipp, G. Une nouvelle méthode pour l'examen direct et immédiat de l'excitabilité faradique des muscles paralysés. [**A new method for direct and immediate examination of the faradic excitability of paralysed muscles.**] *München. med. Wchnschr.*, 1919, **47**, 1342. (*J. de radiol. et d'électrol.*, 1920, **4**, 94.)

The faradic excitability of a muscle severed from its motor nerve persists for a considerable time, as Perthes has already shown, and one may still find, about eighteen months after section of the nerve, a clearly recognizable contraction if the current be applied in sufficient intensity to the naked muscle. But this method is inconvenient; as the examination can only be performed on an anaesthetized patient and an exposed muscle. The author has introduced a happy modification by replacing the tampon electrodes by two sterilized needles which he thrusts through the skin into the muscle to be examined, to a depth of from 8 to 15 mm. The two needles are about 2 cm. apart. Neither operation nor anaesthesia is necessary, and the pain felt by the patient is no more than that from a simple prick. Movement of the needles indicates contraction of the muscular fibres between them, and is evoked by a very weak current. A stronger current produces a motor effect, but even this intensity is much less than that which is necessary when cutaneous electrodes are employed.

S. U. L-B.

MEDICAL SCIENCE

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REVIEWS

DISEASES OF THE BLOOD

The blood in health and various morbid conditions. Dreyer, Bazett, and Pierce report on diurnal variations in the haemoglobin content of the blood as follows: (1) The diurnal variations in haemoglobin percentage met with in man and animals are very considerable and may even reach as much as 30 per cent., while 10 per cent. changes are of more or less common occurrence. (2) The excursions seem to be more marked in individuals or animals with a low haemoglobin content. (3) The smallest variations, i.e. the utmost constancy, is found between 5 and 7 p.m.

Bloch has been investigating coagulation in the light of a novel theory. According to this writer there can be little doubt that calcium is an essential factor. Calcium is normally present in the blood, but nevertheless coagulation does not take place *in vivo.* This is explained as due to the action of citrates, which are also normally present. The citrates neither precipitate the calcium nor diminish its amount, but they do succeed in keeping it in a physical state which prevents any activity. It cannot be accurately stated what this physical state is, but there are reasons for supposing that it is one in which the electrical charge of the calcium ions is neutralized. Normally citrate and calcium are in equilibrium, but the reaction is quantitative and the addition of more of either will inhibit or accelerate coagulation. It is on the latter fact that Bloch's method of estimating coagulability depends. He mixes fresh blood with a measured amount of citrate and then adds samples to tubes containing calcium solution. His 'indices of coagulability' are respectively the ratios of citrate to sodium in the tubes in which coagulation first commences and is complete. The method has not yet had wide clinical application, but Bloch considers it exceptionally free from technical defects and likely to be of great use.

Thomsen, of the State Serum Institute, Copenhagen, describes the following new method of counting the blood-platelets. The blood is drawn by venepuncture and discharged into a specially graduated tube containing ½ c.c. of a 10 per cent. solution of citrate of soda. The blood-platelets will be held in suspension unchanged for at least six hours, while the red and white corpuscles will have sedimented after two to three hours. The number of blood-platelets contained in the citrate plasma is then determined by a Thoma-Zeiss counting chamber for red corpuscles. Thomsen has found that the number of platelets varies in health from 206,700 to 413,400, the usual number being 250 to 300,000.

Bunting describes the structure of the marrow as unlike that of any other tissue. The central artery gives off branches which run straight to the periphery without branching and there open into thin-walled sinuses. The blood from these is collected into veins which empty into the central vein. In the interstices of the sinuses are found the fat cells and the progenitors of the red cells.

Bunting further believes that the force which propels red cells into the blood-stream is exerted by the increase of size in their mother-cells which must precede division into adult erythrocytes. This increase limits the space in the rigid walled marrow cavities and so obliges some of the cells to escape into the venous blood.

Schenk noted the following results from injections of adrenalin, in each case increasing the dose until a distinct rise of blood-pressure occurred. The effect on the spleen was seen to be an output into the blood of lymphocytes, or, in leukaemia, myelocytes and especially of immature cells. In a case of 'pernicious anaemia' a long-continuing toxic effect was produced and was only alleviated by splenectomy. Adrenalin given to splenectomized persons shows no variation in its effects which might be attributed to absence of the spleen. The effect on the red cell count is an increase, but this is entirely due to concentration and passes off with the action of the drug.

Cowie reports that the injection of adrenalin causes an initial rise in the leucocytes followed by a decline within one hour. At the second hour a further rise occurs and may last eight hours. All varieties of leucocytes participate. The red cells show similar rises. In both cases these are interpreted as being purely mechanical in origin.

Rubino discusses the mode of production of poikilocytes with particular reference to the theory that the compression of neighbouring elements is a factor. He considers this theory untenable, and points out that poikilocytosis usually affects cells which show achromia, hyperchromia, anisocytosis, &c., all of which could not possibly be produced by compression and are indicative of some grave upset of haemogenesis which may well be responsible also for the poikilocytosis.

Craik contributes notes on an interesting experiment to elucidate the nature, &c., of polychromasia and 'stippling' of red cells. He gave lead to certain patients affected with benign tertian malaria. This had the well-known effect of producing the cell changes referred to. He found that these cells were especially liable to be affected by parasites. He also noted that a 24-hour parasite was never found in a polychromasic cell, although younger forms were noted. It is therefore apparent that polychromasia disappears soon after the red cell reaches the circulation. Stippling, on the other hand, persisted longer.

Craik considers that the malaria parasite is best able to infect young cells, and that the older have some power of resisting invasion. He explains the infrequent appearance of Schüffner's dots on the hypothesis that these occur only in mature cells and that such cells are comparatively infrequently affected.

Williams has measured the blood loss in parturition and comes to the conclusion that many normal women can lose 1,250 to 1,500 c.c. without apparent ill effect. He is inclined to explain this by the fact that metabolism is, as he states, at a comparatively low ebb during the puerperium. In some cases very much larger amounts are lost with impunity.

Rosenthal has made exhaustive studies of the blood chemistry in a case of haemolytic jaundice, and tabulates 22 conclusions of which the following assist in separating this syndrome from jaundice due to other causes. Lipoid phosphorus was much diminished in the red cells. The bilirubin content of the serum appeared to be an accurate index of the amount of blood destruction. It is increased after adrenalin injections, which is not the case in normal persons. The kidney threshold for bilirubin is very high and five times the normal amount in the serum still fails to affect the output in the urine. The threshold is rapidly lowered after splenectomy. The paper is a valuable storehouse of facts and experiments, but their interpretation is somewhat obscure in many instances.

Gilbert, Chabrol, and Bénard have studied the urea or nitrogen content of the blood in various haemolytic processes. They were aware of the existence of azotaemia, but at first supposed that it might be common to many general diseases. This was not found to be the case, and their final conclusion is that the liver is as definite a urea-forming factory as it is a manufactory of bile, and that the raw material in either case is provided, or may be provided, by the products of haemolysis.

Souques and Moreau have sought for evidence of the haemoclasic crisis in Raynaud's disease, a morbid process having certain obvious resemblances to others of the anaphylactic or auto-anaphylactic group. The evidence they produce is such as circumstances allowed and is not claimed to be complete. Even so it is very important and it suggests the possibility of cure by the usual anti-anaphylactic methods. They find that there are two distinct types of Raynaud's disease, one anaphylactic and accompanied by general symptoms, the other purely local and giving no evidence of haemoclasia. The former is more rare.

Souques and Moreau propose to pursue the study of their cases when the weather is more favourable, hot weather not allowing of such prominent manifestations, even when deliberately provoked by immersion of the hands, as the cold.

Hall concludes as follows from his case of splenectomy for traumatic rupture: (1) There was a considerable leucocytosis for three months. (2) At first all types of cells were increased, later the increase was due chiefly to large mononuclear and transitional cells which the author includes under the term 'endothelial cells'. There was no eosinophilia during the three months of observation.

Anaemia. The subject of severe anaemia complicating nephritis and possibly connected with the degree of nitrogen retention seems to have attracted little or no attention except from French authors. Aubertin and Yacoel add two new cases to those already recorded, of which they summarize 15. The first case was that of a young girl suffering from acute nephritis apparently following influenza. Anaemia was preceded by haemorrhage, but the subsequent course showed that this alone could not explain it. The blood showed red cells below one million, high colour index and polymorph leucocytosis. Anisocytosis and poikilocytosis were present; no mention is made of polychromasia. There were no nucleated red cells. At autopsy the marrow was apparently in a state of suspended activity and was yellow throughout, even in the sternum. The condition of the marrow is not quite easy to reconcile with that of the blood, e.g. one does not get a high colour index from an aplastic marrow. In the second case the anaemia was terminal but was of the same type. The marrow was in a state of regenerative activity.

It is difficult to be at all certain that the nephritis was really anything more than an associated factor in either of these cases, a difficulty which the authors quite appreciate. But they do not seem to have considered the propriety of classing together two cases of anaemia, one with an aplastic and the other with hyperplastic marrow and having nothing more in common than nephritis. A leucocytosis is not unusual in nephritis, so that it tells neither way. The existence of an infective or toxic factor in most cases of nephritis is not disputed, nor the existence of a similar factor in most severe anaemias. On the other hand, the evidence that anaemia causes nephritis or nephritis anaemia is so very slight that it is better, when the two are found associated, to ascribe them to a common cause rather than to the presence of each other.

According to Thiroux, the association of ankylostomiasis, malaria, and syphilis is very frequent in Annam, and gives rise to an exceptionally severe form of anaemia. Although several practitioners regard the condition as inevitably fatal, Thiroux claims that 75 per cent. of the cases are curable, provided that their nature is recognized. The only incurable cases are those in which there is an advanced renal lesion or superadded tuberculosis.

Krumbhaar and Musser conclude that the catalase content of the blood varies according to the concentration of the red cells, and that this ratio is not materially affected by splenectomy or by the various types of anaemia which they studied.

Aplastic anaemia. According to Gorke, assistant at the Breslau University Medical Clinic, who records three cases in syphilitic women following treatment by salvarsan, aplastic anaemia may be produced by salvarsan just as it may be by benzol or X-ray treatment. Aplastic anaemia due to salvarsan is very rare, however, and only occurs in individuals who have an idiosyncrasy as regards salvarsan, possibly in persons of a lymphatic diathesis. In two of Gorke's cases the symptoms were much alike and consisted in severe haematemesis, necrotic angina, numerous ecchymoses on the trunk and extremities, severe metrorrhagia, and intense anaemia. Urobilin was present in the urine only shortly before death. The third case, which recovered, was of a milder character, but the occurrence of haemorrhages from the gums, epistaxis, and necrotic angina indicated its nature.

Pernicious anaemia. Gettler and Lindeman, of New York, report the following results of the chemical and physical analysis of the blood in 32 cases of pernicious anaemia: (1) The non-protein nitrogen, urea, and creatinin values were somewhat higher than normal, this being probably due not to a permanent kidney lesion but rather to the decreased amount of circulating blood. (2) The uric acid was much above normal. (3) The amino-acid content was greatly increased owing to excessive destruction of sugar protein. (4) The blood-sugar was abnormally high. (5) The alkaline reserve was subnormal. The last three results point to the fact that in pernicious anaemia the power of oxidation within the cell has been reduced to an abnormally low level. (6) The refraction and specific gravity were both astonishingly low, indicating deficiency in serum albumin, serum globulin, and fibrinogen. It was slightly raised in a small percentage of cases. This was due to the small increase of non-protein nitrogenous substances and to the presence of normal or slightly increased amounts of inorganic salts.

According to Mensi pernicious anaemia is one of the rarest of children's diseases, only four cases, whose ages ranged from seven months to two years, having occurred among 3,029 children in his medical wards at the Queen Margaret Children's Hospital at Turin. Of 29 cases recorded in children whose ages and sexes are given, 14 were under two years, and 15 above two; 20 were males and 9 females. Apart from syphilis, tuberculosis, and the bothriocephalus, in the great majority it is impossible to find any causal factor. There is a plastic form which is by far the most frequent, and an aplastic form; intermediate or hypoplastic forms have also been described. The prognosis of pernicious anaemia in childhood is most unfavourable. Of 20 cases 16 died, in 3 the issue was not recorded, and 1—Mensi's fourth case—was still alive.

According to Curschmann, of the Rostock University Medical Clinic who records an illustrative case in a woman aged 37, spinal cord disease may precede the changes in the blood in pernicious anaemia by several years, and the spinal symptoms may occur in exacerbations and remissions just like another non-haematological symptom, viz. glossitis, and the changes in the blood itself. This shows that the spinal disease is not the consequence of the severe anaemia like the spinal changes in tuberculosis, carcinoma, &c., but is the product of some still unknown factor which, sooner or later than the spinal symptoms, produces glossitis and anaemia. According to Curschmann the spinal symptoms in pernicious anaemia are by no means characteristic, spastic cases being as frequent as those accompanied by symptoms of disease of the posterior columns.

Williamson records a fatal case of pernicious anaemia with extreme dropsy in a man aged 33 who had had a similar attack five years previously. At the autopsy, apart from a high-grade fatty degeneration of the myocardium the heart was negative. The kidneys showed only fatty changes. Otherwise the findings were typical of pernicious anaemia.

Signorelli reports very fully a case of severe anaemia of pregnancy. The patient was 34 years of age, and her home conditions were quite satisfactory. She had passed through four normal pregnancies; in the first three there had been slight pallor which had yielded to iron. Anaemia commenced at the fifth month of the fifth pregnancy, and she was admitted to hospital five days before normal labour and the birth of a healthy child. There were no abnormalities in the infant's blood.

Parturition was followed by an accentuation of the anaemia due to loss of blood, by retinal haemorrhages, achylia gastrica, subnormal temperature, and diarrhoea. The latter had been present for some weeks, the stools containing blood and mucus. In spite of this the patient made a complete recovery. The last blood examination was normal, and no abnormal red cells were present.

Signorelli concludes that there is no single feature in which the anaemia of pregnancy differs from any other form of pernicious anaemia, and regards the association of pregnancy and anaemia as no more than a coincidence. Nevertheless this case is one of the few in which the direct dependence of the anaemia on pregnancy seems to be well established, and is a valuable addition to the somewhat scanty literature of the subject.

Maggesi reports a sufficiently typical case of pernicious anaemia, of which the most noteworthy feature was the complete absence of megacaryocytes from the marrow. The marrow from the epiphysis and also from the diaphysis of the tibia was studied. No trace of these cells was found in spleen or liver. Since platelets were found in the circulating blood, Maggesi is inclined to doubt Wright's theory that the platelets originate as protoplasmic fragments of the megacaryocytes. He does not definitely support any alternative suggestion.

Although tuberculous pernicious anaemia was first described fifteen years ago, only a few cases have been published, and most of these occurred in patients with acute or chronic pulmonary tuberculosis. Pissavy, Robine, and Saxe report a case in a man aged 32 in whom pernicious anaemia was caused by tuberculosis of the mediastinal and mesenteric glands. The number of red cells fell to 900,000. Nucleated and deformed cells and a few myelocytes appeared before death.

Graham records 23 cases of pernicious anaemia treated by transfusion in patients aged from 20–70. In 13 cases the transfusion was performed within a year of the first symptoms, in six cases the symptoms had lasted from one to two years, and the remainder were of a more chronic type. Direct transfusion from artery to vein was performed in 19 cases, and indirect transfusion from vein to vein in seven cases. Transfusion was performed on 28 occasions, three patients being transfused twice and one patient three times. Graham concludes that though transfusion may cause a remission of the symptoms it cannot cure a case of pernicious anaemia or alter in any material way the nature of the disease. The results of transfusion are always uncertain in any given case, and are not sufficiently consistent or permanent to justify its being urged in all cases of pernicious anaemia which are stationary, progressive, or critically ill, in spite of the usual methods of treatment.

Leukaemia. Cailliau records a case of acute leukaemia in a woman aged 43 remarkable for its rapid course, death taking place after one month's illness. The temperature ranged between 100·4 and 102·2 F. without any remission. There was an entire absence of haemorrhages, which is unusual in acute leukaemia. Other remarkable features were a leucocytosis of 53,000 leucocytes per cubic mm., the presence of numerous myelocytes in the blood, and the absence of any glandular involvement.

According to Dönecke, of the Rostock University Medical Polyclinic, who records a case in a man aged 63, myeloid leukaemia is very rare in advanced life. The reason for this is to be found in the feeble degree of reaction present in the senile leukaemic tissue, especially the bone marrow. The result is that myeloid leukaemia in old age is sometimes associated with a remarkably low leucocyte count, as in Dönecke's case, in which it was only 69,300 as compared with 100,000–300,000 usually found in leukaemia, or still more frequently assumes the form of an aleukaemic myelosis.

Huese reports the case of a man aged 22 admitted to hospital with the diagnosis of cirrhosis of the liver. There was a history of abdominal pain and distension of about six months' duration, and the condition had been aggravated by a fall on the previous day. On admission the abdomen was only moderately distended, and anaemia was not pronounced. On opening the abdomen, however, large clots and partly fluid blood escaped, and the spleen, which was much enlarged, presented a rupture which extended over the whole of the gastric surface. Death took place six hours after the operation, and examination of the blood showed the presence of myeloid leukaemia.

A case of lymphatic leukaemia simulating Mikulicz's disease is recorded by Roessingh. The patient was a girl aged 7 years, who, after symptoms suggestive of influenza, developed a pleural effusion followed by symmetrical enlargement of the lacrymal and salivary glands. After a period of relative improvement the general condition grew worse, the spleen became enlarged, progressive anaemia developed, and death took place, preceded by haemothorax, petechiae in the skin, haematuria, and intestinal haemorrhage. Examination of the blood a few days before death showed haemoglobin 40 per cent. red cells 2,000,000, and white cells 22,000, in which mononuclears predominated. The autopsy showed numerous enlarged glands in the mediastinum and enlargement of the thymus, spleen, liver, and kidneys. On microscopical examination numerous accumulations of lymphocytes were found in the liver, kidneys, spleen, and left pleura.

Fournier reports a case of lymphatic leukaemia with leucopenia (4,000) instead of the usual lymphocytosis. The patient was a woman of 25, and the disease was acute and fatal. Four other cases are referred to as being all that the literature contains. The author might have included English literature and would then have found many more.

Martin and Denis have studied the chemical changes in the blood following X-ray treatment of leukaemia. In their four cases they found (1) that the non-protein nitrogen was extremely high; (2) creatinin values were normal and urea values relatively low. They are therefore forced to the conclusion that there is in leukaemia some nitrogenous body present which eludes our present methods of qualitative analysis. They found the uric acid content of the blood high even when the white cells were falling rapidly in number.

Hodgkin's disease. Under the title Lymphadénie Aleucémique, Tesseyre deals with Hodgkin's disease. He considers this a special anatomical type of a condition which may be in other cases neoplastic, tuberculous, or infective. He considers that Hodgkin's disease never eventuates in leukaemia, whereas the adénie of Trousseau may do so. This latter seems to Tesseyre to be a chronic infective disorder, a chronic septic and generalized enlargement of lymph glands, distinct from other types of lymphadenoma. It has been known to subside after removal of a septic tooth. In a case of Hodgkin's disease reported, the urine is stated to have been 'hémoglobinurique'—a very rare finding if it really denotes haemoglobinuria as opposed to haematuria.

Zoli discusses in some detail the case of a man aged 54 who died with generalized enlargement of the lymphatic glands throughout the body. The primary focus appeared to be the inguinal glands. There was clinical evidence (cough, cyanosis) of mediastinal tumour. The course was very rapid, probably about three weeks. The blood showed no changes of any diagnostic significance. A small piece of tissue removed by the harpoon from a gland showed plentiful connective tissue containing large 'mononuclear-lymphoid' cells, some of which were in mitosis. Autopsy was not permitted. The case is similar to many others reported as lymphosarcomatosis. Without an examination of the blood the diagnosis must have been leukaemia, so that the question arises whether a negative blood examination can be held to exclude this disease. Certainly cases have been reported in which the characteristic blood changes did not appear until late in the disease. Zoli examines all such possibilities and arrives at his diagnosis of lymphosarcomatosis by exclusion. But he preserves a judicial attitude, and admits the extreme obscurity of the whole subject. The conception of lymphosarcoma as a sudden malignancy, not of a part but of the whole of the lymphatic system, requires just those careful and especially complete reports which are still lacking before it can be accepted.

Haemophilia. Terzaghi reports somewhat discursively a family in which haemophilia was associated with a tendency to cerebral haemorrhage, which proved fatal in several cases. This family would appear to exemplify the 'endothelio-plasmatic' diathesis of Weil rather than true haemophilia. There is no definite evidence of the latter disease.

Voncken reports a case of 'local haemophilia', meaning thereby chronic blood-stained discharge from a war wound. This condition was much ameliorated by 'homohaemotherapy', i.e. by the subcutaneous injection of 100 c.c. of blood from a healthy subject. The injection was repeated after eight days.

Rabe and Salomon report the case of a boy, aged 9, who had from birth a marked tendency to spontaneous haemorrhages. The family history was negative. It was found that the blood of this boy would not clot even when kept several days. Nor did it coagulate when heated to 56°. Various experiments were made, but the addition of fibrinogen was the only measure which produced *in vitro* clotting, and even then the clot formed was of poor quality. The authors conclude that the boy's blood contained thrombogen, thrombokinase, and calcium in sufficient amounts, but lacked fibrin. Should he again suffer from an outbreak of severe haemorrhages they hope to induce fibrin formation by the stimulation of a transfusion.

Happ states that there is not yet general agreement as to the necessity of determining blood groups prior to transfusion from mother to child, e.g. in haemophilia neonatorum. After investigation of the blood groups of infants he concludes that the precise group is not determinable before the end of the first year, and, even when determined, is not necessarily the same as the mother's. Accurate tests should therefore precede transfusion at any age, and cannot be dispensed with even in infancy.

Lapage records two new cases of melaena neonatorum treated by intravenous injection of whole blood. The external jugular vein was used, but Lapage states that he should use the superior longitudinal sinus on any other occasion in view of its greater accessibility. The results were excellent, as is usually the case with this form of therapy.

Weil gives a very concise and useful summary of his methods of dealing with haemophilia, and states that he has always been able to arrest haemorrhage and has never lost a case in 50 cases. For external haemorrhage he thoroughly cleanses the wound with saline so that no clot remains. He then applies a dressing soaked in serum. Human serum is best, but any animal serum will give good results. For internal haemorrhage he administers subcutaneously (not intramuscularly) 20 c.c. of serum and repeats if necessary. He injects the same amount one or more days before operation and treats the wound with serum dressing. For continuous preventive treatment he employs a similar injection every two months, and when decided improvement is manifest every three months. This suffices to keep patients free from symptoms, and would also appear to cure some cases, inasmuch as one man, after six years' treatment, gave up attending, but went through five years of war without accident. He is not impressed with possible dangers from anaphylaxis, as he has found these slight and unimportant.

Purpura. Stahl tabulates the following factors productive of purpura: (1) Injury to the vessel walls, which is an essential condition in all cases; (2) scarcity of blood-platelets, not essential, but very frequent; and (3) absence of retractility of the clot and diminished viscosity of the blood, which are not less important than scarcity of blood-platelets. Calcium and fibrin content he finds to have no relation to purpura, as both may be increased. His investigations are based on cases of typhoid fever and of purpura haemorrhagica.

Polycythaemia. Böttner concludes, after the study of a few cases, that it is not profitable to define different forms of polycythaemia, as these differ only in aetiology, the subsequent and compensatory processes being the same in all cases. He differentiates three stages: (1) early, recognizable only by the increased red cell count; (2) marked polycythaemia with redness, cyanosis, other signs; and (3) the final stage with venous congestion and approaching or actual heart failure. He finds the pressure of the spinal fluid usually increased. The figures of his six cases are 220, 260, 170, 210, 370, and 540, all measured in millimetres of water. He has also noted redness of the optic disk with increased diameter of the vessels, a valuable confirmatory sign of polycythaemia. His cases are very few, and their red cell counts not very high.

Tyrrell reports a case of polycythaemia vera in a man aged 45, complicated by slight hyperthyroidism (slight enlargement of the thyroid, exophthalmos, nervousness, and vertigo). The red cells numbered 9,600,000 per cubic mm., the leucocytes 2,500, haemoglobin 125 per cent., and colour index 0·8. Tyrrell has not found another example on record of polycythaemia in which the thyroid was involved.

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DISEASES OF THE LIVER

Pylephlebitis. Carnot and de Léobardy report the case of a man aged 20, admitted to hospital for recurrent haematemesis with the diagnosis of gastric ulcer. In the course of two years he had suffered from various disturbances in the territory of the portal vein, viz. gastro-enteritis and a first attack of haematemesis in October 1917, and indigestion, ascites, and severe haematemesis in September 1918 and January 1919. After admission to hospital in July 1919, he developed anaemia, ascites, and splenomegaly. He had a fourth attack of haematemesis in September 1919, and a last and fatal one in October. The autopsy showed that the successive attacks were due to the development of thrombophlebitis throughout the portal system. The condition was due to infective micro-organisms probably of intestinal origin.

War diet and the liver. Hoppe-Seyler points out that war diet affected the liver in many ways. In the first place, direct damage to it by a defective supply of nutritive material led to atrophy of the parenchyma and diminished power of resistance. Secondly, indirect damage was caused by abnormal products of decomposition in the intestine, resulting from the unsuitable composition of the diet. A too abundant supply of food rich in carbohydrates and cellulose led to the formation of fatty acids which were injurious to the liver when conveyed to it in large quantities by the portal vein. The frequency of diminution or complete absence of hydrochloric acid in the stomach had the same effect, especially as too rapid evacuation was usually associated with anacidity. The bacteria present in the food were consequently not rendered sufficiently harmless. The resulting duodenal catarrh was readily propagated to the bile-ducts. The absence of fat, which is a powerful cholagogue, was of importance. Monotonous vegetarian diet, such as bread, potatoes, cabbage, and turnips, did not have such a stimulating effect on the flow of bile as a mixed diet of meat, fat, and vegetables. Lastly, the effect of mental worry was not to be overlooked.

Cirrhosis of the liver. The occurrence of familial infantile cirrhosis is so unusual that the cases recorded by Bamberger of Chicago and Schuscik of Jena respectively deserve attention. In Bamberger's cases, which occurred in brothers who were born two years apart, the cirrhosis was probably due to congenital syphilis and was first manifested at the age of 10 in one case and 11 in the other. The three children born prior to the elder one, and five born after the younger one were all healthy. The older child did not come under Bamberger's observation, but the younger one showed some improvement under antisyphilitic treatment, though not to the extent of complete recovery, owing to the late stage at which treatment was commenced. Both cases ended fatally after an illness of three years in one case and five years in the other. The autopsy which was performed on the younger child showed hypertrophic cirrhosis of the liver and marked congestion of the spleen.

Schuscik reports the case of a hitherto healthy female infant, aged two years, whose two sisters had died of jaundice at the age of 2¼ years and 2½ years respectively. Repeated attacks of jaundice occurred and were accompanied by enlargement of the liver and spleen. The urine was at first clear and only occasionally contained traces of bile-pigment, but later became very dark and showed a large amount of bile-pigment. During the last two days the stools were completely acholic. The disease proved fatal within seven months, death following influenza complicated by pneumonia. There was no history or evidence of syphilis, tuberculosis, blood disease, alcoholism, or malaria. The autopsy showed hypertrophic cirrhosis of the liver and chronic enlargement of the spleen in addition to pneumonia of the right upper lobe. The only other example of familial infantile cirrhosis of obscure aetiology, according to Schuscik, is reported by Palmer in a brother and sister aged 9 and 10, in whom the autopsy did not reveal any cause for the disease.

Reference may also be made here to the family described by Bramwell, in which four cases of fatal cirrhosis of the liver occurred, the patients being respectively 9, 10, 14, and 14 years of age. All presented the same general symptoms, rise in temperature, jaundice, and ascites. Death took place in the course of three or four weeks. Bramwell thinks that syphilis and alcohol could be excluded, and suggests that the condition was closely related to Wilson's progressive degeneration of the lenticular nucleus.

A fatal case of hepatic cirrhosis remarkable for its latent course and obscure aetiology is reported by Brookman in a man aged 21, who had always enjoyed good health and did not drink to excess. Death, which was preceded by five attacks of haematemesis, occurred after only twenty-four hours' illness and the autopsy revealed advanced atrophic cirrhosis.

Ellis reports a case of cirrhosis in a man aged 35 with enormous dilatation of the superficial abdominal veins, on auscultation of which an exceedingly loud roaring murmur could be heard, while there was a very marked thrill on palpation.

Under the name of 'Senecio disease' Willmot, assistant health officer, and Robertson, government pathologist to the Union of South Africa, describe a form of cirrhosis of the liver due to senecio poisoning. The disease is of dietetic origin, investigations having shown that the threshed seeds and portions of a weed known as *Senecio ilicifolius* and *Senecio burchelli* are frequently sold with wheat and are ground with the wheat grains into meal. The disease has been present in the George and Mossel Bay districts of Cape Province for at least 10 years, during which about 80 cases—many of them fatal—have occurred. The patients invariably belonged to the poorer class of Europeans, whose staple food was bread. The chief symptoms were abdominal pain and vomiting, with ascites. The prognosis is generally bad, but depends on circumstances. At the autopsy the liver is increased in size and a histological examination shows the usual round-celled infiltration met with in cirrhosis of the liver due to other causes.

A case of mesenteric thrombophlebitis as the terminal manifestation of a latent cirrhosis is reported by Cade and Brette. The patient was a man aged 29, who, apart from two violent attacks of diarrhoea in 1917 and 1918, had had no previous digestive disturbances. He stated that he had always been sober, and apart from attacks of malaria in 1918, which were rapidly cured by quinine, had always been healthy. In November 1919 he was seized with extremely violent abdominal pain without definite evidence of intestinal obstruction and died after a week's illness, death being preceded by haematemesis. The autopsy showed thrombosis of both mesenteric veins and secondary thrombosis of the portal vein which had caused a haemorrhagic infarct of the small intestine 85 cm. in length. The cause of this condition was cirrhosis of the liver, which on histological examination was found to be of recent onset.

Jaundice. Cases of grave familial jaundice in the newly born have recently been reported by Prins, Rolleston, and Agnew respectively. In the family described by Prins the first two children were healthy, but after the birth of the second child the mother had a fall on her back and her subsequent children, who were normal at birth, always became very jaundiced on the third day. The first child born after the fall had severe icterus neonatorum, but recovered. The next child also became very yellow on the third day and died a few days later. The same fate befell the twins who were the next to be born. The following child also became very yellow on the third day, and death took place two days later. There was no evidence of umbilical sepsis or of congenital syphilis, and the Wassermann reaction was negative. On post-mortem examination the bile was found to be extremely viscid, but otherwise nothing abnormal was found either on naked-eye or histological examination. Prins attributes this condition to a congenital familial deficiency on the part of the hepatic parenchyma, similar to that which is found in the thyroid when a woman with Graves's disease gives birth to one or more children with myxoedema. Rolleston regards the condition as due to foetal toxaemia of maternal origin and recommends care of the mother's diet and administration of intestinal and biliary antiseptics such as hexamin, salicylate of soda, minute doses ($\frac{1}{20}$ gr.) of calomel, tetrachloride of naphthalene, salol, and guaiacol. He relates the case of a woman who had had recurrent jaundice in three successive pregnancies with fatal jaundice in the infants, and was given hexamin and salicylate of soda in her fourth pregnancy. In the eighth month she became somewhat jaundiced just before the birth of a boy, who was never icteric, and was well ten years later. In the fifth pregnancy she was treated with small doses of hydrargyrum cum creta, but was jaundiced during the eighth and ninth months, and bore a girl who was slightly jaundiced and died of acute gastro-enteritis when seven weeks old. Agnew reports a case of a family in which the second and third child, a boy and girl respectively, died on the third and twenty-fifth day of intense icterus. There was no ground to suspect syphilis, but no autopsy was made in either case.

Chabrol and Dumont report three cases in girls of one family aged 8½, 11½, and 10 years respectively, who in the course of three weeks successively developed a mild attack of catarrhal jaundice. Although spirochaetes were found in the urine in two cases, inoculation of guinea-pigs and the serum agglutination test were negative, so that spirochaetosis icterohaemorrhagica could be excluded. The patient's serum was then tested with various organisms which give rise to catarrhal jaundice, viz. typhoid and paratyphoid bacilli, *B. coli*, and Gaertner's bacillus, but none of the dilutions in 1 : 50 gave positive results.

Similar cases of familial jaundice have been described by Merklen, and the writers also observed two brothers, aged 10 and 11 respectively, who developed jaundice within a fortnight of one another.

According to investigations made by Garnier and Reilly during the war, infective icterus of typhoid or paratyphoid origin is exceptional. Out of more than 1,300 cases of acute jaundice studied by them between November 1915 and November 1918 only four were due to this cause. In each of these cases the temperature chart was exactly like that of a mild attack of enteric fever, from which it differed only by the existence of a slight degree of jaundice. As in such cases jaundice is not the principal symptom, the designation typhoid or paratyphoid infection with icterus is more suitable than infective icterus due to the typhoid or paratyphoid bacillus.

According to Rothschild and Felsen, of New York, in obstructive icterus due to stones, &c., the cholesterol content of the blood is markedly increased, and bears a definite relationship to the intensity of icterus. In other conditions associated with icterus, such as cirrhosis of the liver, acute yellow atrophy, and pernicious vomiting of pregnancy, the cholesterinaemia bears no relation to the intensity of the icterus.

The drop by drop method advocated by Murphy in surgical infections, and later by Chauffard in medical infections, is recommended in the treatment of jaundice by Weil, who employs 45 grm. of sugar and 1·50 grm. urotropin dissolved in a litre of water. The injection should be given so that the patient can absorb it in four hours, and evacuate it in the urine and not in the stools. Weil found the method effective not only in mild infective and toxic jaundice, but also in cholelithiasis, so that an operation was often rendered unnecessary. On the other hand the treatment was of no value in jaundice due to cirrhosis or new growths. Weil therefore suggests that this therapeutic test might be used to distinguish between simple icterus and icterus due to latent cirrhosis.

Minet records a case of chronic cholecystitis in a woman aged 33, successfully treated by intravenous injections of urotropin, the patient receiving three series of injections containing in all 21·25 grm. of urotropin in 15 days. Marked improvement took place after the fifth injection.

Acute yellow atrophy. The increasing frequency in recent years of acute or subacute yellow atrophy of the liver, which was previously regarded as a rare disease, is emphasized by numerous German writers, such as Umber (1) (2), Huber and Kausch, Strauss, Albu, and Versé. Umber (2) states that during the eight years he was at Hamburg he saw only four undoubted cases of this disease, three of which were certainly due to syphilis, whereas, during the following eight years at Charlottenburg he saw ten cases, seven of which occurred in 1919, and four of these in the course of five weeks. These figures are all the more striking as Ewald, in his book on diseases of the liver published in 1913, states that he had not seen a single case in Berlin during the last fifteen years. As regards the aetiology, both Strauss and Fraenkel emphasize the variety of factors responsible for the condition.

In 13 cases observed by Strauss, 4 had relatively recent syphilis, 2 of whom had had an intensive salvarsan treatment shortly before the onset of their symptoms, in one case there was an otogenous sepsis, and in 3 others gastro-intestinal disturbance. Both Umber (2) and Albu attach great importance to the frequency of gastro-intestinal disturbance, which they attribute to the character of the war diet. The gastro-intestinal catarrh spreads to the bile-ducts and sets up cholangitis, which these writers regard as a preliminary stage in acute or subacute atrophy of the liver. Cases following gastro-intestinal disturbance are also reported by Huber and Kausch. On the other hand, Fraenkel states that his observations do not confirm the theory of a gastro-intestinal origin for this disease, and maintains that the question can only be settled by prolonged bacteriological and experimental investigations. Syphilis, to which formerly much aetiological significance was attributed, does not appear to figure so prominently in the recent cases, Umber (2) remarking that nine of his ten Charlottenburg cases were undoubtedly not syphilitic. It is also noteworthy that though, as in the past, more females are attacked than males, in 5 cases reported by Versé neither a coexistent nor recent pregnancy could be incriminated. As regards the clinical course the most striking features described by recent observers are the greater frequency of recovery (Umber (1), Huber and Kausch), the occurrence of abortive cases (Umber (2)), the relative frequency of ascites (Albu, Fraenkel, Huber and Kausch, Strauss, and Umber (2)), and the presence of anasarca in one case (Albu). The establishment of the diagnosis during life by an excision of a portion of the liver and histological examination occurred in several cases. (Umber (1), Strauss, Huber and Kausch). Exploratory laparotomy was performed in Umber's case owing to the presence of severe colic, a symptom which has never been previously described in atrophy of the liver, and is attributed by him to cholangitis. Strauss's case occurred in a woman aged 32 who for three years had suffered from periodic attacks of abdominal pain accompanied by jaundice and colourless stools. When seen by Strauss, in addition to jaundice ascites was present. As no improvement followed removal of three litres of fluid by paracentesis, laparotomy was performed on the possibility of there being obstruction of the common bile-duct. This supposition was not verified, but only adhesions of the omentum with the duodenum and gall-bladder were found. The surface of the liver was nodular and traversed by sulci between which cyst-like nodules projected, which, on histological examination, proved to be the remains of the liver parenchyma. In Huber and Kausch's case, which occurred in a woman aged 26, jaundice and ascites rapidly developed after eating sardines. Obstruction of the portal vein was diagnosed and laparotomy performed. The liver was small and of a dark brown colour. A small portion of it was excised and histological examination showed that the parenchyma was to a large extent destroyed. The ascites at first reaccumulated, but as the result of drainage complete recovery took place.

According to Weigeldt, who records a fatal case in a man aged 27, in whom about half the neutrophil polymorphonuclear leucocytes showed vacuolar inclusions in the protoplasm, the blood picture in acute yellow atrophy is as follows: The red cells and haemoglobin are increased. There is a moderate leucocytosis (10,000–30,000) and a marked increase of the polymorphonuclear neutrophil leucocytes with deviation of the Arneth count to the left. Weigeldt denies the blood any value in differentiating acute yellow atrophy from phosphorus poisoning, infective jaundice, or other forms of icterus.

According to Robin, Weil, and Bith, ascites is an uncommon event in the course of **hydatid disease** of the liver. They record a case in a woman aged 23 who gradually developed symptoms of dyspepsia about an hour after food, pain in the region of the liver, and progressive increase in size of the abdomen. Examination showed a striking contrast between the emaciated supra-diaphragmatic region and the infiltrated and distended infra-diaphragmatic region. The lower limbs were oedematous, the abdomen distended, and there was a considerable degree of ascites. The liver was much enlarged in all its dimensions, but no enlargement of the spleen was detected. Weinberg's test was positive, and there was an eosinophilia of 20 per cent. A diagnosis of hydatid cyst was confirmed by laparotomy, and complete recovery took place. Ascites in cases of this kind is attributed by the writers to a mechanical or inflammatory obstruction of the inferior vena cava or more frequently perhaps of the portal system.

As a general rule the duration of **cancer of the liver** is short. In fulminating cases it may prove fatal in one to one and a half months, but its usual duration is between three and five months. In some cases it is prolonged for six or seven months. Generally speaking the duration of the cancer is related to the patient's age; below 40 it is fatal in less than two months, between 40 and 70 its average duration is three to six months, and after 70 it is often not fatal until five, eight, or twelve months.

Ribadeau-Dumas and De Laulerie, from whose paper this information is obtained, report a case of primary cancer of the liver without cirrhosis in a man aged 72, in whom the first symptoms developed about five years before his death, and suggest that his age was a factor in the duration of the disease.

Pryce reports a fatal case of peripheral multiple neuritis associated with primary malignant disease of the liver in a woman aged 70. The case presented many features resembling those of diabetic neuritis, but differed in the absence of diminished tactile sensibility and of perforating ulcers of the feet. There was no autopsy.

Angioma of the liver. Alivisatos, of Athens, records the case of a woman aged 52, with a history of dyspepsia of ten years' duration, who for the last five months had been losing flesh and suffering from dysphagia and anorexia. On examination she presented a tender tumour high up in the epigastrium. The symptoms suggested either a new growth in the upper part of the lesser curvature in the neighbourhood of the cardiac orifice or an old ulcer with perigastritis. These diagnoses, however, were excluded by the negative results of radioscopy. Exploratory operation revealed the presence of an isolated angioma of the liver, which was removed, and complete recovery took place.

Primary **hepatomata** are rare in children, only 16 authentic cases having been collected by Rolleston in 1912. Wollstein and Mixsell report a case in an infant aged 4 months. The tumour grew to be very large, emaciation, cachexia, and death resulting six months after a nodule had been first noticed. A metastasis was found *post mortem* in the upper lobe of the left lung. Histologically the tumour was an epithelial growth, probably congenital in origin.

In a paper based on the study of 114 cases of **gall-bladder disease** seen during the past eight years, Cheney, of San Francisco, states that he regards the history as the most valuable aid in the recognition of gall-bladder disease. He distinguishes four distinct groups of cases with the following histories: (1) Recurring attacks of colic with good health between. This is the most frequent group, to which 45 of the 114 cases belong. (2) Recurring attacks of colic with more or less constant indigestion between. This group was represented by 25 cases. (3) Chronic stomach trouble with subacute gall-bladder attacks. 34 cases belonged to this group. (4) Chronic stomach trouble with no history pointing to the gall-bladder over long periods of time. 10 cases belonged to this group.

Carl Wessel's investigations into the relations of cholelithiasis to achylia (*Hosp.-Tid.*, 1918, **61**, 1233–56) have thrown much light on the pathology and treatment of gall-stones, and Rydgaard's paper, based on material provided by Professor Rovsing's hospital and private clientele, follows to a certain extent the same lines, amplifying and checking Wessel's observations. Rydgaard found that among 158 cases of gall-stones, the diagnosis being confirmed by operation, and cases associated with cancer and gastric ulcer being excluded, there were 18 with hypochylia, and 58 with achylia. The proportion of cases with one or other of these conditions was thus 47·4 per cent. Like Wessel, he found that gall-stone achylia was comparatively common among men, the combined incidence of hypochylia and achylia being 73 per cent. in men, and only 42·4 per cent in women. The significance of this finding was largely discounted by the fact that a comparatively high proportion of the men were over 60, at which age achylia is common apart from gall-stones. Grouping his cases according as they were jaundiced or not, Rydgaard could find no appreciable difference in the incidence of hypochylia and achylia. But the size and situation of the gall-stones were important, for when the stones were confined to the gall-bladder the incidence of achylia was only 25 per cent., whereas this figure was more than doubled when stones were found in the cystic and common bile-duct alone or in conjunction with stones elsewhere in the biliary system. The incidence of achylia was 35 per cent. for small stones in the cystic duct, 62·9 per cent. for large stones or of a size to obstruct the cystic duct, and 70 per cent. for complete obstruction of this duct. These observations confirm Hohlweg's hypothesis that closure of the cystic duct provokes achylia. This occurs with increasing frequency the more complete the obstruction of the biliary passages is, and its development has in some cases been shown to coincide with closure of the cystic duct.

Rydgaard then reviews, in the light of his and Wessel's investigations, the hypothesis, advanced by Rovsing in 1915, that many patients whose gall-bladders are put out of action develop incontinence of the sphincter papillae, which must favour infection. Out of 64 septic cases (Rydgaard's and Wessel's combined) 33 were associated with total achylia, and 42, or 66 per cent., with achylia or hypochylia. Wessel found that among his 25 cases of achylia or hypochylia there were 15 septic cases. Rydgaard does not confirm this observation, as of his 66 cases of achylia or hypochylia 39 were not septic. The two series of observations can, however, be brought more into line if in Rydgaard's series the numerous non-septic cases with hydrops or total occlusion of the gall-bladder be excluded. For it seems probable that in these cases the gall-bladder was shut off from infection before the onset of the achylia. In a table indicating the frequency of hypochylia or achylia in relation to the micro-organism infecting the biliary system, Rydgaard shows that coccal infection is seldom, and coliform infection is often, associated with achylia. The coliform cases numbered 35, the coccal cases only 11.

Discussing the hypotheses of Hohlweg, Rost, Simnitzky, Wessel, and Rovsing, as they appear in the light of recent observations, Rydgaard remarks that, granted that hypochylia and achylia are due to the gall-bladder being put out of action, the processes by which this sequence occurs are still obscure. Hohlweg assumes that when the gall-bladder is put out of action the bile escapes in a continuous stream into the intestine, thereby provoking achylia by a reflex mechanism. In 1919, Rovsing elaborated the hypothesis that, as only a proportion of the patients with obstruction of the cystic duct develop achylia, this depends on another factor, incontinence of bile. The subjects of cystectomy should accordingly be classified as they acquire continence or not of bile. The incontinent develop achylia because the acid contents of the stomach, when they reach the duodenum, are not adequately neutralized by bile. The unneutralized HCl acts on the wall of the duodenum, setting up reflex achylia. Between this class and that in which there is complete continence of bile and no achylia, there are intermediate classes with less sharply defined characteristics.

Turning to the therapeutic deductions to be drawn from all the available data, Rydgaard argues that gall-stones should be operated on as soon as they give rise to symptoms. Otherwise there is great risk of the sequence: occlusion of the cystic duct, achylia, sepsis. The physiological importance of the gall-bladder having been demonstrated, it follows that cholecystotomy is superior to cholecystectomy, as the former may cure the patient of his achylia as well as of his gall-stones. Cholecystotomy may indeed be followed by relapse. So may nephrotomy for renal calculus. But this does not prove nephrectomy to be the better operation for calculus.

In Cheney's cases of gall-bladder disease gastric analysis was made 81 times. In 26 the total acidity was under 40, and in 12 of these under 20 with complete loss of free HCl ; in 38 cases the total acidity was over 60 ; all the other 17 analyses were within normal limits. There were therefore more patients found with hyperacidity than with hypo-acidity in this series. Cheney concludes that gall-bladder disease may be associated with either hyperacidity or hypo-acidity, but while hyperacidity is as frequent in ulcer or chronic appendicitis as in gall-bladder disease, hypo-acidity, and especially achylia, are found with gall-bladder disease more often than in any other morbid condition except cancer. The discovery, therefore, of achylia with a dubious history of chronic gastric trouble is very suggestive of gall-bladder disease.

Fravel gives the following account of gastric findings in 61 cases of bile-tract infection with and without stones verified by operation. 16 showed an absence of free hydrochloric acid, and 45 showed free hydrochloric acid, 29 of less than 20, 11 within the bounds of normal, and only 5 above the normal. 11 cases showed a total acidity of 50 or more, and 39 a total acidity of less than 40. No cases were included that showed any associated organic stomach condition, such as cancer or ulcer, a malignancy of the gall-bladder, or pancreas. Fravel suggests that the hypo-acidity may be the result of the loss of a hormone that is secreted by the normal gall-bladder, which loss inhibits the secretion of hydrochloric acid, or that it may be due to a disturbance of intermediate chloride metabolism.

Furno states that Grocco, in 1901 and several subsequent communications, pointed out that in cholelithiasis, especially during the colic, a pleural rub might be heard on one or both sides, and that sometimes a pleural effusion might occur, which was almost always on the right, rarely bilateral, and always due to the primary liver condition. Pleurisy is most frequent in cholelithiasis, but it also occurs in other diseases of the liver, such as cirrhosis, hydatid disease, and carcinoma. Furno now records three cases of pleurisy secondary to syphilitic disease of the liver which were cured by specific treatment. The frequency of pleurisy secondary to disease of the liver as compared with diseases of the other abdominal organs, such as the spleen, kidney, pancreas, and stomach, is attributed by Furno to the fact that four-fifths of the lymphatics originating in the liver pass into the thorax and supply the parietal and visceral pleura.

Ricaldoni, of Montevideo, applies the term 'sialorrhoeic form of cholelithiasis' to those cases which are characterized by profuse salivation. This phenomenon did not occur during the violent attacks of colic but during the subacute stage, irrespective of the age of the patient or the duration of the disease. In some cases the saliva was fluid and clear and in others thick and frothy. The salivation usually occurred after the attacks of colic, but in one case in which the patient had suffered for several years from cholelithiasis the salivation used regularly to precede the colic. Ricaldoni regards the salivation as a reflex phenomenon similar to that seen in stenosis of the oesophagus and hyperchlorhydria.

Albu draws attention to the greater frequency of infective cholecystitis leading to the formation of gall-stones and cholangitis, especially among young persons, in recent years, and attributes this occurrence to intestinal disturbances caused by war diet. During the last five years he has seen seventeen cases of acute and subacute cholecystitis in patients under 20 years of age, including two cases of cholelithiasis in children. On the other hand, Hoppe-Seyler does not think that the formation of gall-stones has been increased by the war diet. He points out that gall-stones must be present for some time before they produce symptoms. Moreover, a diet rich in albumin has been incriminated with producing a more abundant formation of cholesterin in the organism, so that war diet would have rather the opposite effect.

Babcock draws attention to the possibility of cholecystitis in every person with heart disease of whatever nature who complains of indigestion or subdiaphragmatic pain. The diagnosis is arrived at as follows: in passive hepatic congestion from heart disease the liver preserves its natural and characteristic outline, unless this is prevented by adhesions or by changes due to cirrhosis. When not cirrhotic, but merely congested, the left lobe is palpable and tender as well as the right. Moreover, when secondary passive congestion of the liver exists, one is sure to find evidence of venous stasis in the organs and tissues. On the other hand, when cholecystitis is responsible for enlargement of the liver, it causes a characteristic alteration in Riedel's lobe; another sign of gall-bladder disease is Ewald's area of cutaneous hyperaesthesia over the right tenth and eleventh intercostal nerves posteriorly.

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BOTULISM

Epidemiology. According to McCaskey, *B. botulinus* is of very wide distribution. Although outbreaks are rare, they are probably much more frequent than is supposed. He reports an outbreak of seven cases, four of which were fatal, at Decatur, Indiana, following the consumption of canned beans.

C. G. and A. F. Jennings and Haas describe an outbreak of botulism in a Detroit suburb, the source of the toxin being a glass jar of ripe olives. Of eight persons who ate the olives five died, one escaped, and two were slightly affected. The writers estimate that there have been at least 40 recognized outbreaks of botulism in the United States, with 150 cases and 97 deaths.

Sisco reports an outbreak of botulism which occurred in January 1920 in an Italian family living in the Bronx, New York City. The source of the toxin was a glass jar of Californian ripe olives. The olives, consumed as such and as part of a salad, caused the death of six of the seven members of the family who ate them. As in the Detroit cases reported by Jennings and Haas, the patients who vomited at the onset died sooner than the others. Mental clearness, maintained until shortly before death, was strikingly characteristic. All the patients were drowsy and somewhat comatose immediately before death.

Four fatal cases of botulism occurring at Boisé, Idaho, from eating canned asparagus are reported by Thom, Edmonson, and Giltner. All cultures of the Boisé organism—a strain of *B. botulinus*—had a characteristic offensive odour which was clearly evident in the canned material. The writers point out that decomposition occurring in a can or jar properly packed, exhausted, and sealed is necessarily anaerobic. When physical evidence of such decomposition is present, the material should be destroyed, not eaten.

Randell reports an outbreak at Florence, Arizona, of 10 cases, 5 of which were fatal, following the consumption of canned beetroot.

Bitter, of the Kiel University Institute of Hygiene, records three outbreaks of botulism which occurred at Kiel between June 1918 and June 1919. Eight persons were affected and three died. Two of the outbreaks were due to the consumption of pickled herrings and one to ham. *B. botulinus* was isolated from the herrings and ham in most of the cases. Bitter has also collected all the cases of botulism which have occurred in Germany between 1897 and 1913, during which period there were 70 outbreaks with 302 cases and 51 deaths. Only 41 outbreaks with 198 cases and 17 deaths occurred in Prussia up to 1913. Ham, smoked meat, and bacon were responsible for a quarter of the cases. Sausages were as frequent a cause as ham, blood-sausages being the most dangerous. About 17 per cent. of all the cases were due to fish, including lobsters. Of vegetable foods Darmstadt preserved beans were the only ones which gave rise to botulism. About a quarter of the cases followed the consumption of some food the name of which was not stated. The mortality varied considerably according to the nature of the food. The highest mortality—52 per cent.—was associated with the Darmstadt beans, which were eaten as a salad, that is, without being cooked or heated. Ham, smoked meat, and bacon caused a mortality of 19 per cent., and sausages a mortality of about 17 per cent. The mortality due to other articles of food was remarkably low, owing to partial destruction of the toxins by heating before the meal was taken. The mortality caused by fish and lobsters was about 10 per cent. The mortality among cases in which the nature of the food was not specified was 13 per cent.

Dickson, Burke, and Ward state that the number of cases in which canned foods have contained the botulinus toxin is comparatively very small. The greater number of outbreaks has been caused by home-canned products, and it is only in a few cases that commercially canned goods have been at fault. They point out that if all canned food is boiled before it is eaten any possible danger of poisoning with botulinus toxin will be avoided, as the toxin is destroyed by boiling.

Symptomatology. The appearance of the throat in botulism, and the features which distinguish it from diphtheritic paralysis are described as follows by Vernieuwe, director of the Ghent University Clinic for Otorhino-laryngology. (1) Absolute dryness of the mucous membrane of the mouth, pharynx, and larynx is constant in botulism, frequently giving rise to atonic ulcers, but is absent in diphtheritic paralysis. (2) Paralysis of the palate, which is found in both diseases, is usually unilateral or at least predominates on one side in diphtheritic paralysis, whereas in botulism complete paralysis of the palate is the rule. (3) The course of the disease will probably clear up the diagnosis, although certain symptoms are common to both diseases, such as albuminuria, muscular weakness, cardiac atony, anaemia, and loss of reflexes. (4) Diphtheritic paralysis can be best distinguished from the paralysis of botulism by a careful examination of the ocular manifestations, the differences being as follows: (i) in botulism accommodation and the sphincter pupillae are generally affected simultaneously if not always in the same degree. In diphtheritic paralysis, on the other hand, the reaction of the pupil is unaffected in the great majority of cases; (ii) the external muscles of the eye are very rarely affected in diphtheritic paralysis (in 1 case per 1,000 according to the literature), whereas in botulism involvement of the external muscles as well as ophthalmoplegia interna is not uncommon; (iii) in botulism the ocular paralysis often appears on the first day, more frequently on the second or third day, after the consumption of the tainted food, whereas diphtheritic paralysis does not occur till much later, as a rule about four weeks after the sore throat; (iv) the duration of the paralysis in botulism exceeds that of diphtheritic paralysis, the paralysis lasting from four to eight weeks in diphtheria as compared with five to eight months in botulism.

Vernieuwe also emphasizes the resemblances between the symptoms of botulism and those of atropin poisoning, which is characterized by restlessness, dryness of the throat from diminution of the salivary secretion, anxiety, irritability, visual hallucinations, and dilatation of the pupils. But there is never any ophthalmoplegia externa in atropin poisoning. This symptom is peculiar to botulism, which also causes absolute paralysis of accommodation.

The ocular manifestations of botulism are described by De Saint-Martin, of Toulouse, who observed four cases in soldiers which had developed after eating smoked trout. Although any bacteriological or experimental investigations were impossible under the circumstances, there was no doubt as to the diagnosis. Two of the men were not seen until twenty days, and the other two until forty-two days, after the onset. The patients showed not only the ocular symptoms usually described as typical of botulism, namely, ptosis, mydriasis, affection of accommodation, and movement of the eyeballs, but also congestion of the optic nerve and retina and narrowing of the visual field. According to De Saint-Martin, changes in the optic nerve and retina in botulism have only once been described before, namely, by Gutmann in 1891, and may be regarded as a manifestation of the congestion of the entire optic nerve similar to that of the vagus, phrenic, bulbar nuclei, and anterior cornua of the cord described by Mesnil and Marinesco. The narrowing of the visual field is probably due to lesions in the retinal cells, similar to those described by Marinesco in the mesocephalic nuclei.

For further information regarding the symptomatology of botulism, reference should be made to Dickson's monograph (vide *Medical Science*, 1920, **2**, 470–2).

Treatment. McCaskey emphasizes the importance of active catharsis as early as possible. As experimental work has shown that fatty substances apparently combine with the toxin, markedly attenuating if not destroying its virulence, he recommends that a cathartic oil such as Ol. Ricini should be given in full doses early and repeatedly.

As there are at least two types of *B. botulinus*, which are distinct as far as their toxin-antitoxin relationships are concerned, Dickson and Howitt, of San Francisco, recommend that a polyvalent antitoxin should be employed and should be given in large doses intravenously, as the amount of toxin ingested is unknown.

Recent reports, however, as to the use of botulinus antitoxin are disappointing. In Randell's case it was of little or no effect; Sisco speaks of it as inconclusive. Jennings and Haas record that 42 c.c. were injected intravenously in one case without any apparent effect, and 20 c.c. in two injections in another case which recovered. This patient's illness, however, was so slight that the serum probably did not have any influence on his recovery.

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J. D. R.

THE RADIOLOGICAL TREATMENT OF MALIGNANT DISEASE

In a report presented to the International Congress of Surgery on July 22, 1920, Regaud, Director of the biological laboratory at the Radium Institute, Paris, tried to place himself in the surgeon's position, conceiving that though modern methods tend towards abandonment of surgical removal of a cancer, yet for the present surgery in some form holds the field. He divided his subject into three parts: (1) The rational foundations of radiotherapy in cancer. (2) Factors determining the choice of method (removal, radiotherapy). (3) General principles of technique; selection of the irradiation method and mode of its use. Each of these was further subdivided and the answers to a number of questions of first importance were indicated. It was pointed out that there is an increasing tendency to use X-rays of shorter and shorter wave-length in order to approximate to the extremely short gamma-rays, and that in X-ray therapy of malignant tumours advance has proceeded largely as such shorter (and therefore more penetrating) waves have been used. Of course in radio-diagnosis great penetration is not necessary, so that exponents of the two main objects with which rays are used are becoming differentiated to a great extent. Next followed consideration of the part played by filters in reducing the highly complex beam produced by the X-ray bulb to a more or less homogeneous beam. Such a highly penetrating beam falls off in intensity with greater regularity as it passes through the tissues and exerts a greater selective action upon cells. Regaud insisted that in our present state of knowledge no practitioner ought to attack a new growth by X-rays—even if that growth were cutaneous—unless his installation were sufficient to yield within a relatively short time a considerable dose of radiation filtered through at least 4 or 5 mm. of aluminium. In the case of radium, the gamma-rays alone may be used (as when radium, radium emanation, or mesothorium is enclosed within a platinum tube 0·6 mm. thick), or the gamma- and beta-rays (as in radium puncture or the use of naked glass tubes of emanation), or the alpha-, beta-, and gamma-rays (as in use of 'active deposit' needles or solution). It is not quite certain that he is right, but Regaud believes that in all cases where a caustic action of beta-rays is not desired the tendency is to use greater and greater filtration of gamma-rays as it is of X-rays. The question is then asked, 'How do X- and gamma-rays act upon the living tissues?' Some little penetrating and therefore easily absorbed rays have a general caustic action, but the more penetrating rays have an 'elective cytocaustic action'. Thus by using X-rays filtered through 7–8 mm. of aluminium it is possible to bring about a complete and definitive disappearance of a subcutaneous round-cell sarcoma or lympho-sarcoma without leading to any cutaneous reaction other than a definitive epilation of hair or beard; the cytocaustic action has involved the sarcoma cells and the generative cells of the hair bulbs alone. There is a long scale of radio-sensibility for animal cells, ranging between the most radio-sensitive (such as certain sexual and leucocytic cells) and the least radio-sensitive (such as muscular fibres and nerve cells). The radio-sensibility, too, is a property of the nucleus and is inherent in certain states or temporary physiological periods of cell life, the most important and best known of which is the state of reproduction. Another period of heightened sensibility corresponds to the maximum metabolic activity of the nucleus in cells which have a secretory function. And since such cell division and nuclear metabolism are neither continuous nor prolonged states, it follows that the same cell or generation of cells manifests alternating radio-sensibility and radio-resistance. The effect on the cell is shown by every grade from early death to slight reparable injury. The dead cells are removed by autolysis or phagocytosis, but the intercellular substances are resistant and absorbed slowly. Arguing from these premisses Regaud asserts that 'X- and gamma-radiations of very short wave-length are elective poisons for nuclear chromatin, upon which, as is known, heredity depends. Hence the rays suppress or suspend cellular reproduction in a tissue.'

The next question is, 'Why and to what degree are neoplastic tissues radio-sensitive?' And the answer is found by the author in the indefinite reproduction of cancer cells. Since X- and gamma-rays of very short wavelength are poisons antagonistic of cell reproduction, they are curative agents for cancer. Nevertheless, each variety of neoplasm corresponds to a definite position in the scale of radio-sensibility, and on this subject our knowledge is far from complete. The practitioner must definitely exceed the lethal dose for the tumour cells and fall short of severe injury to the normal cells. In a highly radio-sensitive tumour (e.g. round-cell sarcoma) the range is wide and a suitable dose is easily chosen. In a little radio-sensitive new growth (e.g. squamous-cell carcinoma or epidermoid epithelioma) the range is narrow, the suitable dose is difficult to reach, and radiotherapy is not without danger. The removal of cancerous cells and intercellular substances after irradiation is along the same lines of autolysis and phagocytosis that characterizes removal of irradiated normal cells, but if the growth be ulcerated, or if alpha- and beta-rays be used, there is a certain diffuse disintegration in which normal cells are no more protected than the neoplastic cells.

The second part of the report dealt with the choice between surgery and radiotherapy in cases recognized as curable by surgery, with radiotherapy in inoperable cancer, and with combinations of surgery and radiotherapy. In cancers of skin Regaud insists that the surgeon at the present time has no right to operate on rodent cancer, but that when glands are involved the question is more open; he then thinks X-rays should not be used, or should be combined with radium-puncture or with surgery.

The radio-sensibility of connective tissue and lymphoid malignant new growths is as follows, the varieties of tumour being given in descending order of radio-sensibility: lymphosarcoma, large and small round-cell sarcomata, mixed-cell sarcoma, giant-cell sarcoma, myxosarcoma, spindle-cell sarcoma, fibrosarcoma, chondrosarcoma, osteosarcoma. Hence the choice between surgery and radiotherapy, even if the surgery be possible, must be influenced by this fact. If one of these tumours be small, limited, easily accessible, and therefore operable without great destruction of tissue, it will nevertheless be better to treat it with an appropriate and extensive irradiation, whatever be its variety or situation. But if it be large, diffuse, inaccessible in its deeper parts, the only varieties that may be treated with rays are those described above as highly radio-sensitive, even if removal mean amputation of a limb. In all such cases, whether radiotherapy or surgery be ultimately adopted, a preliminary microscopical diagnosis is essential.

On the other hand certain operable cancers ought not to be treated by rays, e.g. carcinoma of stomach or intestine and radio-resistant squamous-cell carcinomata, the former from reasons of accessibility, the latter because, according to most authorities, radio-technique at the present day at most leads to temporary regression of the tumour. In the case of squamous carcinoma of the cervix uteri and alveolar carcinoma of the breast, choice between surgery and irradiation is still uncertain. With regard to the former, Regaud holds that the most suitable cases for operation are those also most suitable for radium treatment, and suggests that the following course should be adopted in a series of carefully reported cases, viz. the best cases of cervico-uterine cancer, those in which there are no palpable signs of extension beyond the uterus, ought to be treated first of all by radium and a few weeks later by surgical removal. If the radium therapy has been effective the statistics of recurrence after Wertheim's operation ought to show considerable improvement; in the opposite event the patients, at any rate, will not have lost the benefit of surgical intervention. Cancers with infiltration of the parametrium ought to be reserved to radium therapy, which, if it be properly carried out, ensures at least as long a survival as surgery. In the case of carcinoma of the breast he advocates a similar procedure.

While dealing with this part of the subject Regaud discusses the question whether radiotherapy favours dissemination of cancerous cells. He believes that such is not the case, but is ready to allow that with a bad technique the local conditions may be made worse and that under any circumstances it may favour the development of already existing foci at a distance. He quotes cases in which local regression of a tumour was followed by growth of metastases elsewhere, but maintains that in this respect radiotherapy is no worse than surgery. Nevertheless he allows that the growth of such metastases is apt to be 'a little more rapid after radiotherapy than after surgical removal, possibly because absorption of substances resulting from the destruction of the cells by the rays exerts a favouring influence upon, or the substances are utilized in the development of, collections of cells that were hitherto latent'. He goes on to add, 'such facts should not be laid to the charge of radiotherapy. They should remind us incessantly that the cancers are local diseases in their early stages alone; that removal and radiotherapy have only a local curative value.' The removal of portions of tissue for biopsy he maintains is essential to diagnosis and sound treatment, but the biopsy should be rendered harmless by asepsis and careful suture in the case of a closed tumour and by a preliminary sterilizing X-radiation in cases of ulceration and infection.

Passing to consider inoperable cancers, Regaud points out that in such cases the radiologist is usually begged to intervene. Even then intervention is sometimes undertaken with definite chances of success, but more often the sole perspective is amelioration of the patient's condition. In this connexion there are certain contra-indications to radiotherapy. Such are cachexia, cancer of intensely rapid growth, varieties of growth which are particularly refractory (e.g. branchioma, melanotic sarcoma), risk of perforation of a hollow organ and formation of a fistula, bony necrosis (particularly of jaw), symptoms of visceral metastasis. Severe local infection is also a contra-indication, as radiotherapy under such conditions leads to intense, perhaps fatal, septic intoxication or to rapid growth of metastases. In many situations it is possible to postpone irradiation until the sepsis has been diminished by suitable dressing, but in uterine cancer there is always some uncertainty whether a thickening of adnexa is partially inflammatory or solely malignant. Special care must therefore be exercised to exclude chronic peri-uterine sepsis, and, if this cannot be done, radium treatment must be carried out with great caution.

In considering the question of cicatrization of ulcerated lesions as the result of treatment Regaud states that the rapidity of cicatrization is a function of the patient's age, general state of health, extent of the surface to be repaired and the quality of ray used, and the method of its administration. An epithelioma treated with soft X-rays or beta-rays of radium is associated with injury to the surrounding normal elements: a radiodermatitis occurs, and cicatrization, if it occur, is slow and the scar tissue is poor. The best method for obtaining a good scar is to give the total required dose of irradiation within a short period (a few days) and then allow repair to proceed without further radiotherapeutic intervention. Regression in size of the tumour is almost invariable when the dose and quality of irradiation have been right, but the rate and degree of regression vary within wide limits.

Dealing with combinations of surgery and radiotherapy, post-operative and pre-operative radiotherapy are considered. The former meets with the author's disapproval. Post-operative radium therapy is often illusory or even dangerous: it ought to be reserved for such cases as may be treated with precision, e.g. at the summit of the vagina after hysterectomy or in the cavity resulting from resection of the upper jaw when a recognizable focus of neoplasm is present. Post-operative radiotherapy was not conceived on absolutely sound principles and has not justified itself fully. It is at least as fair to consider surgery an adjuvant of radiotherapy as radiotherapy ancillary to surgery. Pre-operative radiotherapy rests on a sounder basis, for it diminishes the risk resulting from ulterior development of disseminated cancer cells, it is more effectively carried out than when cicatrization has occurred, it does not interfere with the subsequent surgical operation, and if properly conducted does not impede cicatrization of the operation wound.

In some cases a partial removal associated with radiotherapy is indicated, as in carcinoma of breast or large superficial sarcoma. There are advantages in not requiring the body to remove a large mass of irradiated tissue, but in removing it surgically, even though complete removal may not be possible. And, lastly, in certain cancerous conditions of the digestive tract, larynx, bladder, uterus, &c., a preparatory surgical operation may render possible a form of treatment by rays which otherwise would be impossible.

In the third part of the report Regaud takes as his text this rule: 'for efficacy and harmlessness of radiotherapy it is necessary that all parts of a tumour should receive equal and sufficient amounts of radiation as far as possible simultaneously or within a relatively short interval.' He considers the application of the law of inverse squares under X-ray therapy and radium therapy, the influence of absorption by the tissues and filtration, the difference between superficial applications and buried tubes. After considering cases specially suitable for X-rays and those specially suitable for radium, he sums up as follows: 'In fine, if an even irradiation over a considerable surface but without any considerable depth be required, X-ray therapy should be chosen; if, on the other hand, a very powerful irradiation be required over a circumscribed area, especially if the neoplasm be thick or deep, preference should be given to radium. . . . Almost without exception rational radiotherapy of a malignant tumour will call for a judicious combination of X-rays and radium.' So far as concerns the relative values of radium, mesothorium, or radium emanation, the former two are suitable for external application, and for insertion into foci of considerable size the latter is invaluable in that radiation can be applied by means of extremely small needles.

Referring to the general conduct of radiological treatment in a case of malignant disease, Regaud points out that when a man is subjected to repeated doses it is the same *normal* cells that are irradiated but not the same *malignant* cells. Hence the integuments and other normal cells become successively less radio-resistant owing to cumulative action, whereas the malignant cells may not have altered in radio-sensibility. Indeed, in palliative radiotherapy one of the limitations of beneficent action of the rays is precisely the limit of integrity of the general tissues of the tumour and its neighbourhood.

So far as concerns the distribution of doses he recommends that the whole extent of the neoplastic territory, including lymphatic areas manifestly affected, should receive, equally, the dose judged to be effectual. This treatment should be as nearly simultaneous as possible (10–15 days) over the whole area to avoid overgrowth at a non-radiated spot in compensation for diminution in volume at an irradiated spot. In respect of the amount of irradiation to be administered it is, unfortunately, not at present possible to speak with precision. Broadly speaking, 'one should give in each case the maximum compatible with the integrity or rapid recovery of the normal tissues, while at the same time affording these the greatest possible amount of protection'. And in any case where the aim is cure and not palliation alone an attempt should be made to give the entire dose at a single sitting and avoid the necessity of giving a second or a third dose of greater intensity.

With reference to intensity and time of application he insists that the same dose as measured by milligrammes and hours produces different results if quantity be small and time be large, or if, on the contrary, quantity be large and time small. In actual practice at the Radium Institute of Paris, good results were found:—

In tubular epithelioma (squamous carcinoma without cell nests) of the cervix uteri when treated with intensities of 100-150 microcuries of radium emanation destroyed per hour and per focus.

In round-cell sarcoma and lymphosarcoma with intensities of 50–100 microcuries per hour.

In carcinoma of the breast with intensities of 25–50 microcuries per hour.

In epidermoid epithelioma (squamous carcinoma with keratinization) and in connective tissue tumours rich in fundamental substance with intensities of 5–25 microcuries per hour.

This paper has been abstracted at length, since it is, in the reviewer's opinion, one of the most judicial and judicious statements of the question that have appeared. To a very great extent it is based upon actual experiment and the views expressed command assent. On the other hand it is possible to doubt some of the premisses and hence the conclusions obvious or concealed to which Dr. Regaud is conducted. Thus he repeats on at least three occasions that the action of the rays is *local*. No doubt in a sense this is true, but the mere facts that the intensity falls off according to the law of inverse squares, and that a circulation passes through the irradiated part, indicate that a general effect of irradiation has to be reckoned with. These distal effects of the rays may well be of great importance. Quite apart from the fact that at some distance an 'elective cytocaustic action' must become converted into an 'elective cytostimulative action', just as at some distance an irritant which induces inflammation becomes converted into a stimulus which induces repair, it is possible that the lymphocytic changes following on irradiation may indicate a fundamental process which is general and not local. Without wishing to be dogmatic, there is some reason for believing that patients showing little lymphocytic fall in the circulating blood upon irradiation react better to the treatment than those in which a marked fall occurs. And just as Dr. Regaud advises combined X-ray and radium treatment, so it may be that a combined beta- and gamma-ray treatment would give better results than either of these alone. The premiss that action of the rays is purely local has a cramping effect.

Probably, too, in considering the action of rays upon cells, attention has been riveted too much upon the nucleus. There is no doubt that in a highly irradiated tissue one may find tracts of cytoplasm without trace of nucleus, or nuclei in varying stages of disintegration. But this does not mean that cytoplasm is unaffected. On the contrary, cytological changes are often considerable when our histological methods fail to reveal nuclear changes. And, further, radiation of the thyroid body, which is often very effective in some varieties of Graves's disease, teaches us that functional changes are induced by irradiation which are unaccompanied by recognizable histological changes. For even after exposure over a prolonged period to as much gamma-radiation as that from 5 grm. of radium bromide the thyroid of an animal often presents a remarkably 'normal' appearance.

Dr. Regaud gives no indication as to the position occupied by the columnar cell in his scale of radio-sensibility. The matter is important in view of the frequent occurrence of carcinoma of the rectum and other parts of the gastro-intestinal tract. According to experiments carried out by the reviewer, it is at the opposite end of the scale to dry squamous epithelium. Nor does he try to explain the different behaviour towards irradiation of squamous-cell carcinoma starting in a dry or a moist situation respectively, and, more important, gives no indication of the modification in dosage that is demanded. Moreover, in conjunction with his valuable data on intensity, we should have liked to hear his views on the time factor in dosage. And to conclude a criticism which in reality expresses great admiration for the report, is it not the case that the patient has much to say in determining the outcome of an irradiation? Reference has been made above to the possibility that different lymphocytic behaviour under irradiation accompanies different reaction of neoplasm; in another place the reviewer has made reference to a woman in whom cancer of one breast had been cured by X-rays and cancer of the opposite breast responded unusually well to radium: and in experiments now being conducted, two cats were exposed to the gamma-radiation from 5 grm. of radium bromide for 90 hours and the histological pictures presented in the two cases were far from identical.

Lastly, Dr. Regaud employs the word 'Curietherapy' in contrast to 'Roentgenotherapy', following the suggestion originally made by Bordier. There is much to be said for coining special terms in the case, but would not 'curiation' and 'radiation' be more euphonious?

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W. S. L.-B.

THE IMMEDIATE SURGICAL TREATMENT OF GASTRIC AND DUODENAL HAEMORRHAGE

In *Medical Science*, 1919, **1**, 178, a review of gastric and duodenal ulceration was given from the surgical point of view. A number of other communications have appeared since, among which there is an account by Finsterer, of Vienna, of 24 cases operated upon immediately on account of severe and persistent haemorrhage.

There has hitherto been an agreement among both physicians and surgeons that under such circumstances operation should be delayed until the patient has become somewhat less anaemic. Surgical interference in the face of recent and continuing haemorrhage has been unfortunate; surgeons have found it difficult to do anything at once quickly and effectually. Statistics have been continually put forward to show that few, varying from 3 per cent. to 17 per cent., actually die of the haemorrhage; obviously the accounts vary according to the number of early cases included; the late cases, such as those noted by Finsterer, which do not die of perforation or cancer, die of haemorrhage. If cases suffering from gastric and duodenal ulceration were submitted early to operation, deaths from haemorrhage would be avoided; to this it can be objected that the operation of gastro-jejunostomy has been overdone of late.

Finsterer's cases were all of long standing; they had had gastric disturbance for years, with repeated attacks of haematemesis and melaena, of increasing severity. They had had long courses of medical treatment, not only of the out-patient kind, but also of full medical treatment in hospital. Whilst under the latter, haemorrhage increased, and they were transferred for the surgical operation when in several of the cases the pulse could no longer be felt at the wrist. Under medical treatment in hospital was included prolonged stay in bed, exclusive rectal feeding, and the injection of various serums. Of the 24 cases operated upon in a stage of acute anaemia, in 16 there followed a good recovery with permanent arrest of the gastric or duodenal haemorrhage, and in most, complete relief from dyspepsia. Of the 8 deaths only one was attributable to a failure to arrest haemorrhage (Case V); in 4 (Cases II, IX, XV, and XVII) death was due to the acute anaemia, the patients being moribund at the commencement of the operation; 3 deaths were due to other causes. In one case death occurred 18 days after the operation owing to acute colitis (Case XIX). Case XVI was the subject besides of tabes and bronchitis, Case XXII of pyonephrosis. During and after the operations the low blood-pressure was vigorously countered by saline infusions, injections of camphor, lowering of the head, bandaging of the limbs, &c. For anaesthesia, the local injection of novocain was mainly used, preceded or not by the injection of morphin, and supplemented by open inhalation of small amounts of ether. It was found necessary to restrict both the novocain and particularly the morphin owing to the danger of impairing the respiration; in such extremely anaemic patients $\frac{1}{10}$ of a full dose had as much effect as a full dose in a full-blooded patient. The total amount of novocain should be restricted to 50–60 c.c. of a 0·25 per cent. solution. Anything more than 1 c.g. of morphin before the operation may be dangerous; Case XVII had 2 c.g. and this dose appeared to determine the arrest of the respiration; it is better on the whole to dispense entirely with morphin. The most important point shown is that a wide excision of the ulcer offers the best means of arresting the haemorrhage. When the ulcer has penetrated into the pancreas, the stomach or duodenum is separated, leaving the floor of the ulcer. No attempt is made to remove this, but haemorrhage from the pancreas is arrested by transfixing ligatures, passed deeply. Then the peritoneum is sutured over, or a drainage-tube used. Not only is it an error to attempt to remove the deep part of the ulcer which has penetrated, but also failure follows upon the application of a ligature to the artery assumed to be supplying the ulcer.

In one or two of the earlier cases, profoundly anaemic from duodenal haemorrhage, a ligature was applied close above the pylorus, followed by gastro-jejunostomy. Then one end of a strip of gauze was applied to the anterior wall of the duodenum, so as to make direct pressure upon the ulcer through the intact wall. The other end of this tampon was brought out through the epigastric incision, and the direct pressure on the duodenal ulcer assisted by an external pad and firm bandage. A consideration of the following cases will embolden a surgeon to operate at once, even although the patient is extremely anaemic. Cases X, XI, and XII may be specially singled out for notice.

Case I. A woman aged 46 had had gastric trouble for five years, and she had twice undergone hospital medical treatment. She had become worse, with frequent vomiting of coffee-grounds material, tarry stools, marked wasting, and anaemia. For 9 days before the operation she was for the third time under hospital medical treatment. Blood in the stomach rendered X-ray examination of no service. At the operation the pulse was very small, 120 in rate. There was found a carcinomatous ulcer of the lesser curvature; nearly the whole of the stomach was removed and the cardiac end joined to the duodenum. A tube was inserted into the jejunum for 4 weeks. There was a good recovery; 6 months later the patient was in good health and had gained 20 kilos in weight.

Case II. A man aged 26 had had gastric trouble for 3 years with hunger pain, pain in the back, and stools often quite black. After 6 weeks of hospital medical treatment he had soon to be readmitted. Whilst being again treated medically he had a sudden relapse, vomited blood, and had frequent stools, at first tarry, then showing almost unaltered blood. At the operation the radial pulse could no longer be felt, the carotid pulse-rate was 150. The stomach was found empty, the whole of the small intestines and colon full of blood. A duodenal ulcer had penetrated into the pancreas. A ligature was applied so as to exclude the pylorus, a gastro-jejunostomy established, and a large tampon applied outside the duodenum as mentioned above. Death followed 10 hours later, and it was found that an old-standing duodenal ulcer had penetrated through the pancreas into a large branch of the coeliac axis.

Case III. A man aged 49 had had gastric trouble for 2 years, severe pain for 2 months, also several fainting attacks during the previous 3 weeks, with haematemesis and melaena. For the last 3 days there had been nearly unaltered blood in the stools in spite of medical hospital treatment. At the operation he was very pale, the pulse-rate 110–120, small. Perigastric adhesions were exposed and the intestines found full of blood. A duodenal ulcer, 2 cm. from the pylorus, had penetrated the pancreas. The pylorus was excluded by ligature and gastro-jejunostomy performed; 10 days later he was discharged from the surgical ward. Two years after the operation he had gained only 4 kilos and still had gastric trouble, but had not lost blood again, either by vomiting or by stool.

Case IV. A maidservant aged 21, who had had gastric trouble, was admitted with melaena for hospital medical treatment. Under this she had haematemesis, several fainting attacks, and at last passed almost unaltered blood in the stools. At the operation she was very anaemic, the pulse 120, very small. The small and large intestines were found full of blood. There was an ulcer at the back of the duodenum the size of a bean. She was treated in the same way as Case II, the plug being gradually withdrawn. She made a slow but good recovery.

Case V. A man aged 55 had had syphilis 25 years before, and gastric trouble for 12 years, during which he had repeatedly been under medical hospital treatment. During the last course of treatment he had become rapidly worse with haematemesis and melaena. He vomited blood on the day of operation, and he became very weak with a pulse-rate between 120–130. There was an ulcer on the lesser curvature, the size of a crown-piece; the coronary artery was ligatured on either side of the ulcer, and gastro-jejunostomy established; vomiting of blood in large amount followed the operation and he died in two hours. Two large pancreatic arteries had opened into the floor of the ulcer, unconnected with those which had been ligatured.

Case VI. A man aged 41, who for a year had had signs of a duodenal ulcer and had undergone repeated courses of dieting, three days before the operation was seized with faintness followed by tarry stools. He was pale and weak with a pulse-rate of 92. There was a small callous ulcer four fingers' breadth from the pylorus, and the small and large intestines were filled with blood. The surgical operation was similar to that in Case II; blood continued in the stools for 3 days; the tampon was gradually withdrawn. Five years later he had a good colour but had gained little weight in spite of care as to diet, and he frequently had pain even on a milk diet.

Case VII. A maidservant aged 23 had had for the previous two years fainting attacks with black stools, and had been under medical treatment in hospital for three months. On the day before the operation there was sudden haematemesis with fainting, and three motions at intervals of two hours containing blood. On the day of operation she vomited bright blood and there was fresh blood in the motions. She was markedly anaemic, the pulse small and 120 in rate. There was an ulcer at the upper margin of the pylorus, which was not stenosed, and below this a small duodenal ulcer. The treatment was the same as in the former case, and there was a slow recovery; after 24 days she was returned to the medical ward; there was no further report.

Case VIII. An engineer had had for four years repeated attacks of left renal colic. For one year he had had occasional attacks of gastric pain with black stools. On the day of operation there was a sudden vomit of one litre of blood and gastric fluid, also melaena; at the same time the abdomen became acutely tympanitic with an absence of peristalsis and an epigastric splash. The stomach was found enormously distended, reaching to the pelvis; it had to be punctured, and 2 litres of blood and gastric fluid were removed. Then the stomach and colon being raised, it was found that the duodenum had been compressed by the mesentery (see *Medical Science*, 1920, **3**, 145).

There was an adhesion between the plica duodenojejunalis and the descending colon, which was pushed forward by a renal tumour. After posterior gastro-jejunostomy the case healed without any return of haemorrhage, and four weeks later left-sided nephrectomy was done for pyonephrosis. Four years after this the patient had a good colour, he had increased in weight, there had been no more gastric disturbance nor haemorrhage.

Case IX. A man aged 36 had had gastric trouble for two years, and for eight days before operation he was under medical hospital treatment, during which haematemesis and melaena continued until the radial pulse could no longer be felt, and the carotid pulse, scarcely palpable, had a rate of 140–150. The stomach was found full of blood, there was more than half a litre of clot. Two large ulcers near the cardia had penetrated the pancreas. The stomach was separated from the pancreas exposing an open pancreatic artery, also a branch of the gastric artery, which were transfixed and ligatured. The ulcers of the stomach were then excised. He died 14 hours after the operation.

Case X. A man aged 22 had had gastric trouble for two years; for two weeks he was under medical treatment in hospital which entirely failed. There was severe haematemesis on the morning before the operation, the radial pulse could no longer be felt, the carotid pulse was small, the rate 160. The man was apparently moribund. An ulcer of the first part of the duodenum had penetrated the pancreas, the stomach was dilated, the small and large intestine contained blood. The ulcer was separated from its floor in the pancreas, which was transfixed and ligatured. The upper part of the duodenum and some of the stomach were excised, an end to side union was effected, and a drain down to the head of the pancreas. There was little discharge and the wound healed well. Two months later the man was still pale but had gained 8 kilos; two years after the operation he had gained 22 kilos, was in good health and back in military service.

Case XI. A woman aged 48 had had for 10 years gastric trouble, and in spite of faintings and black stools was as late as two weeks before operation declared by a Professor of Medicine to have been suffering all the time only from nervous hyperacidity. Three days before operation she was admitted for medical hospital treatment on account of severe haematemesis and melaena; the treatment failed. At the operation the patient was very thin, exsanguine, the radial pulse not felt, the carotid pulse, 150, scarcely perceptible. The stomach and intestines were full of blood, an ulcer on the lesser curvature had penetrated the pancreas. The separation of the stomach exposed in the floor of the ulcer a patent branch of the splenic artery and another of the gastric artery, other branches being thrombosed. Two-thirds of the stomach was excised, and an end to side anastomosis made; the floor of the ulcer was drained. There was slow recovery from the anaemia. Fourteen months after the operation she had gained 15 kilos and had no more of any of the disturbances previously termed nervous. 2½ years after the operation she was able to undertake house-work and to put up with limitations of food consequent on the war.

Case XII. A man aged 41 had had gastric disturbance for five years, and had often vomited; latterly the vomit had contained blood; a year before he had three weeks of medical hospital treatment; he had wasted from 73 to 48 kilos. For a week prior to the operation he was again under medical hospital treatment after a sudden attack of haematemesis, fainting, and blood in the stools. At the operation he was extremely anaemic, the radial pulse could be scarcely felt, the rate being 130–140. There was a large callous ulcer, 2 cm. across and 1 cm. deep, on the middle of the lesser curvature, and the induration had extended into the gastro-hepatic omentum towards the oesophagus. In the floor of the ulcer were three openings of branches of the right gastric artery. The ulcer and a portion of the stomach were excised. A year later he had had no further gastric trouble and had increased 8 kilos in weight in spite of a shortness of nutritious food. The same report was made 2½ years after the operation.

Case XIII. A woman of 47 had had gastric disturbance with occasional attacks of pain and black stools. For a month before operation she was under medical hospital treatment, during which faintings, haematemesis, and much blood in the motions continued until the pulse-rate had become 116–124. A duodenal ulcer 3 cm. from the pylorus, the diameter of a crown-piece had penetrated the pancreas. The duodenum below and the small intestines were full of blood. The upper part of the duodenum with half the stomach was excised, and an end to side anastomosis was made. Pallor and giddiness persisted for a long while; a year after the operation she was in good health and had gained 20 kilos; 2½ years after she said she had never felt better in her life.

Case XIV. A man aged 35 had had gastric attacks for 10 years; haematemesis and melaena continued under medical hospital treatment. He was wasted, very anaemic, the pulse-rate 120. The stomach was thickened, not dilated; 3 cm. from the pylorus a duodenal ulcer had penetrated the pancreas; there were also two callous ulcers on the lesser curvature. The duodenum and small intestines were full of fresh blood. A large branch of the pancreatico-duodenal artery opened into the floor of the ulcer. The treatment was similar to that in the previous case. A year later there had been no more trouble and there was a marked increase in weight.

Case XV. A man aged 33 had had gastric disturbance with haematemesis for 5 years. A week of medical hospital treatment previous to the operation failed to arrest haematemesis and melaena, also there was bronchitis and impaired resonance at the bases of the lungs up to the 7th ribs. At the operation he was very thin, had a deadly pallor, the radial pulse was no longer to be felt, the carotid pulse was very small, the rate 130–140. There was blood in the stomach and intestines down to the transverse colon. A callous duodenal ulcer close to the pylorus had penetrated the pancreas, and had eroded into a large branch of the pancreatico-duodenal artery. The treatment was the same as in the preceding case, but the patient died two hours after the operation. The peritoneal cavity was found normal.

Case XVI. A man aged 57, after syphilis 36 years before, was suffering from tabes, advanced arteriosclerosis, emphysema and chronic purulent bronchitis. For 6 weeks he had vomited after almost every meal, also at night, and had wasted to 37 kilos. Two days before operation he had severe haematemesis, which was repeated, also melaena. The stomach was found dilated, its wall thickened, and on the anterior wall was an ulcer of long standing which had penetrated the liver. There was blood in the stomach and intestines. The stomach was excised, leaving the floor of the ulcer in the liver, which was drained. The pulse improved for two days, then there were signs of pneumonia on the right side, and he died 3 days after the operation. The post-mortem confirmed the observations made during life.

Case XVII. A senior lieutenant had had gastric disturbance for many years. A year and a half before gastro-jejunostomy had been performed for a duodenal ulcer. The symptoms recommenced after the operation and continued under medical treatment, marked hyperacidity and melaena being noted. On the day of operation there was a sudden collapse with severe and repeated haematemesis until the radial pulse could no longer be felt, the carotid pulse-rate was 146, and the patient was apparently moribund. The stomach was found empty, the jejunum and colon full of blood. There was a callous duodenal ulcer 2 cm. from the pylorus; the gastro-jejunostomy opening was on the back wall ·15 cm. above the pylorus. There was an afferent jejunal loop 20 cm. in length; at the side of the anastomosis was a large peptic ulcer which had eroded into the middle colic artery. Excision of the upper part of the duodenum and stomach with side to end anastomosis and implantation of the afferent loop of the jejunum into the descending loop was proceeded with. Respiration stopped three times, attributed to an excessive dose of morphin in extreme anaemia. The third arrest occurred as the abdominal wall was being closed; after 1½ hours of artificial respiration, the heart also stopped. The only thing noted at the post-mortem was mitral stenosis.

Case XVIII. Male aged 33. Of 6 brothers, 4 had gastric trouble; of 6 sisters, 3 were similarly affected.

The patient had suffered for 10 years from periodic attacks. For 10 days before operation he was under medical hospital treatment during which haematemesis and melaena increased and the pulse became quick and weak. The stomach and small intestine were filled with blood; there was a duodenal ulcer, and one the size of a crown-piece on the lesser curvature which had penetrated the pancreas. Half the stomach and upper part of the duodenum were excised. Six days after operation he was attacked by dysentery endemic in the hospital. He survived this and gained 20 kilos in 4 months. A year and a half after the operation he was in very good health, free from all his previous symptoms.

Case XIX. A man aged 49 had had gastric disturbance for 14 years; he had had repeated treatment at Karlsbad; he became worse on military service. Under hospital medical treatment haematemesis and melaena increased with diarrhoea. He was very anaemic, with a pulse-rate of 110–120. The stomach and small and large intestines contained blood; an ulcer on the lesser curvature had penetrated the gastro-hepatic omentum. Half the stomach was excised. Diarrhoea continued, there were 20–30 motions the next day with mucus, and death occurred 18 days after operation. The stomach wound had healed; the mucosa of all the colon was a dark red with many spots of necrosis; the mucosa of the lower ileum was injected but without necrosis.

Case XX. A senior official aged 36 suffered on military service from recurring attacks of cholecystitis with jaundice during three years. Whilst in hospital under medical treatment for cholelithiasis and wasting he collapsed suddenly and passed a mass of bright red blood. The next day he had two severe attacks of haematemesis. There was found a large duodenal ulcer which had involved the bile papilla and had penetrated into the pancreas; an alternative supposition was that a cancer of the head of the pancreas had penetrated the duodenum. The treatment was similar to that of Case II. Haematemesis recurred once only, the night after the operation; there was primary union, but an obstinate diarrhoea delayed improvement for two months. A year later he had gained 16 kilos in weight and was able to take all food. There had been no return of jaundice or of haemorrhage, which disposed of the cancer supposition.

Case XXI. A woman aged 49 had for many years periodic attacks of gastric pain and one year previously a severe haematemesis. Four days before operation she fainted and passed almost bright blood, later decomposing blood, in the stools. The anaemia increased, also the pulse-rate to 130. The stomach was dilated and filled with blood, and the whole of the small intestines contained blood. There was an ulcer on the lesser curvature the diameter of a crown-piece, four fingers' breadth from the pylorus, which had penetrated into the gastro-hepatic omentum. In the duodenum was a scar of an ulcer. Two-thirds of the stomach and upper part of the duodenum were excised. She recovered slowly from the anaemia but was able to take all food; some diarrhoea checked the increase of weight but was attributable to food restrictions. Two years after the operation she was quite well.

Case XXII. A man aged 60 had had gastric disturbance for 30 years and had been treated repeatedly for dilatation of the stomach. Four days before operation there was a sudden attack of haematemesis followed by melaena, which increased under medical treatment. He was wasted and anaemic, with a pulse-rate of 110. He had besides chronic purulent bronchitis with abundant expectoration. The stomach was found enormously dilated, thickened, and full of blood. In the duodenum close to the pylorus was a callous ulcer which had penetrated the pancreas. The ulcer having been separated there was left a deep excavation in the pancreas, which was transfixed and ligatured. After excision of the upper part of the duodenum and half the stomach, followed by the typical anastomosis, the abdomen was closed except for a drain down to the ulcer. So far as this operation was concerned there was a good recovery, but 6 weeks later the left kidney had to be drained for pyonephrosis, complicated by insufficiency of the right kidney. He died two months after the above drainage of the kidney.

Case XXIII. A man aged 29 had been repeatedly treated at Karlsbad during four years for gastric disturbance, acid eructations, and hunger pain. During the three years preceding the operation there were several attacks of haematemesis and melaena. On the day of the operation he vomited a litre of bloody fluid and passed bright blood in the stools; the pulse-rate was 110. There was a large and thickened stomach, and blood filled the small and large intestines. A duodenal ulcer 2 cm. from the pylorus had penetrated the pancreas, from which when the ulcer was separated a large artery spurted. The treatment was the same as in the previous case. He recovered, and a year later was quite well.

Case XXIV. A woman aged 22 had had during the previous year repeated attacks of gastric pain, followed by melaena. Gastro-jejunostomy was done soon after the commencement, but the symptoms continued and increased under medical treatment until she was very anaemic, with a pulse-rate of 130, small. She was very restless, passed bright blood in a stool just before the operation, and had haematemesis on the operating table. The small and large intestines were filled with blood. In the descending loop of the jejunum, just beyond the gastro-jejunostomy opening, was an ulcer the size of a bean. No signs of ulceration were found elsewhere, either in the stomach or duodenum. The ulcer was transfixed and ligatured, then the gastro-jejunostomy anastomosis was closed. Nine months later she was well under a careful diet and had had no more haemorrhage.

Finsterer, H. Ueber akute Magen- und Duodenalblutung und ihre chirurgische Behandlung. *Deutsche Ztschr. f. Chir.*, 1920, **158**, 44.

W. G. S.

CHRONIC EPIDIDYMITIS WHICH IS NOT TUBERCULOUS

There is need for caution lest a hasty diagnosis that a patient is suffering from tuberculous epididymitis involve a prognosis that he is subject to tuberculosis.

To a clinical examination chronic epididymitis may present the characteristic signs of tuberculous disease. The epididymis after removal may appear to the naked eye infiltrated by nodules undergoing caseation and forming excavations containing cheesy pus, indistinguishable so far from tubercle. At the same time the vas may be found thickened by a moniliform arrangement of nodules, having a similar appearance when cut into. Yet a careful microscopic examination may fail to discover, either in the nodules or in the walls of the excavations, any sign of giant cells or other evidence of tuberculous disease. Hence no statement as to tubercle, however vague and qualified, should be based upon the clinical examination of the epididymis and vas, but only upon a microscopic examination after removal.

It is impossible to exclude a gonorrhoeal urethritis as the ultimate origin, and the term 'nonspezifische', employed by two of the writers to be referred to, is not good. In a few the introduction of a foreign body into the urethra is a possibility. There is, perhaps, now less difficulty in deciding that there has been no syphilitic infection. But even although there was a primary gonorrhoeal urethritis, yet in later stages there are found only staphylococci in the urethral discharge. An acute gonorrhoeal urethritis may be complicated by gonorrhoeal prostatitis, and then by gonorrhoeal epididymitis. But later on, when only staphylococci are found in the urethra, there may set in a chronic enlargement of the epididymis and vas, indistinguishable clinically from tubercle, yet due to staphylococci. The discovery of staphylococci in the urethral discharge will suggest that these organisms are the cause of the chronic epididymitis.

The diagnosis of chronic septic epididymitis is more likely to be made when catheterism has been employed for the relief of retention following enlargement of the prostrate or spinal injury. Yet even in such cases, if the epididymitis is chronic in its course, rather than acute or subacute, so much attention has been given to tuberculous epididymitis, that there is a tendency to assume that tubercle has supervened.

Less commonly, chronic non-tuberculous epididymitis is haematogenous in origin, due to staphylococci, streptococci, or *Bacillus coli.* Staphylococci and streptococci may gain entrance through a boil, scratch, or septic wound, and although commonly the metastatic infection shows itself in bones and joints, it need not do so, but may attack the kidneys or epididymis. Staphylococcal nephritis may spread to the bladder, and the patient, experiencing a chill and pain in the back, followed by cystitis, attributes his trouble to a cold or to influenza. The same applies to a nephritis or cystitis set up by *Bacillus coli.*

A chronic sepsis induces symptoms resembling those caused by tuberculosis, such as wasting, night sweats, and loss of weight and strength. Since the disease commonly spreads down the vas from the bladder, a thickening and tenderness may be noted on rectal palpation of the prostate and vesiculae seminales. Whilst exceptionally a chronic septic epididymitis may present the relatively painless, craggy enlargement regarded as characteristic of tuberculous disease, yet generally it tends to be more tender, is more often complicated by the formation of a hydrocele, and the inflammation spreads more readily to the scrotum. The hydrocele may contain yellowish-brown fluid, attended by a progressive thickening of its wall. Even although the case be really one of tubercle complicated by septic inflammation, suppuration, and scrotal sinuses, yet it is only by microscopic examination that the diagnosis of tubercle can be properly established.

The necessity for differentiating tuberculous from septic epididymitis does not relate to treatment; the excision of the epididymis should be carried out whenever it continues enlarged, lest the testis become involved; if the scrotum has become invaded castration is required in order that the patient's general health may be benefited.

The following are among the cases described by Dorn:

(1) A man aged 34 had had, 7 years before, gonorrhoea followed by epididymitis. The left epididymis had become slowly enlarged to form a cap over the testis, the vas was swollen and in places nodular, neither were painful and the testis was normal. The right epididymis and vas were less enlarged but hard. His doctor diagnosed tuberculosis. The urine was clear with a few leucocytes in the sediment. No tubercle bacilli or gonococci were found and the bladder and kidneys were normal. After rest the swellings subsided leaving both epididymes indurated.

(2) A man aged 42 had been healthy, without glandular enlargement, but his parents and several sisters had died of tuberculosis. His urine was turbid from leucocytes and contained gonococci, but a swelling of the right epididymis appeared to follow upon a contusion of the scrotum; the swelling persisted for 7 months, when the right epididymis formed a cap over a normal testis, hard, somewhat painful, and slightly irregular; the vas was the size of a lead pencil with nodules; there was slight prostatitis with nodules and enlargement of the vesiculae; there was also a small hydrocele, the size of a pigeon's egg. The left side testis and epididymis were normal. On a diagnosis of tuberculosis castration was done; examination disclosed chronic inflammation, but no sign of tubercle.

(3) A man aged 50 had had pleurisy without much fever 8 weeks before, when, without explanation, the left epididymis became indurated and painful, the vas was swollen, and there were leucocytes in the urine. The preceding pleurisy suggested a diagnosis of tubercle, and castration followed. The epididymis showed most changes in the head, less in the tail. It contained 4 chronic abscesses the size of cherries, with yellow pus; the wall of the abscesses, other parts of the epididymis, also the vas, showed chronic inflammation; there was no sign of tubercle, no giant cells, no caseating foci.

(4) A man aged 53 had had typhoid fever 36 years before, and 29 years before a chill and cystitis, followed by painful micturition, which lasted 6 months; two years before he had had inflammation of the lungs and recently an attack of influenza. Upon this followed swelling of the left epididymis, and 14 days later of the right epididymis. He had a slight cough, night sweats, loss of appetite. At the right pulmonary apex were signs suggestive of phthisis. In the scrotum were two hydroceles the size of hen's eggs, with the skin and dartos free. The right epididymis was enlarged and hard, the corresponding vas was normal, also the vesicula, but the prostate was tender. The right hydrocele contained clear fluid.

The right epididymis was removed; it contained several discrete nodules the size of peas; on microscopic examination there was no sign of tubercle.

(5) A man aged 68, suffering from emphysema and bronchitis, also from prostatic enlargement, began 3½ weeks before to have pain in the left testicle. The urine contained pus and a trace of sugar. A swelling formed in the left scrotum which involved the scrotal wall, the vas was thickened up to the external abdominal ring, and there was a hydrocele. On laying open the tunica vaginalis the epididymis appeared to present in its head several caseating foci, whilst the testis was normal. After removal, a microscopic examination exhibited chronic inflammation and no sign of tubercle. Subsequently there was an attack of epididymitis on the right side, a hydrocele also formed but subsided after conservative treatment although clinically similar to that on the right side.

(6) A man aged 54 had always been well, but his wife was suffering from lung trouble and a child had died of abdominal and pleural inflammation. Six weeks before, the right testicle had become increasingly swollen and painful. There was on the right side a hydrocele the size of a goose's egg; the epididymis, especially the head, was enlarged and painful with nodules; the tail was the size of an almond. The vas of that side, also the left testicle, the prostate, and the vesiculae were normal. A diagnosis of tubercle was made, the hydrocele laid open, the testis found normal, the epididymis and vas excised. Chronic inflammation without any evidence of tubercle was found.

(7) A man aged 28 was shot through the left lung and was in hospital for 7 months. There was much cough, yellow expectoration, fever, night sweats, and loss of 20–25 lb. in weight. The right epididymis was enlarged and indurated, also the vas; the left side remained normal, also the urine and prostate were normal to examination. But on a diagnosis of tuberculous epididymitis, epididymectomy was done; two indurated nodules in the epididymis showed chronic inflammation but no tubercle.

One of the cases noted by Kappis was as follows: A man aged 33 had had a slight attack of painful micturition 5 years before. Two years later a painless enlargement in the left scrotum gradually developed. On applying for life insurance he was advised by the medical examiner to have the swelling removed. In the left scrotum was a swelling the size of a goose's egg, indurated but painless, consisting of the enlarged epididymis; the testis could not be plainly distinguished by palpation. In the head of the epididymis were nodules of a size between a pea and a cherry. After removal the enlargement was found due to simple chronic inflammation; there was no sign of tubercle or syphilis. Obviously the results of examination had an important bearing on the life insurance.

Kroll reported 14 cases, 13 unilateral, all on the left side, and one bilateral but not simultaneous, first the right side followed by the left some days later. Three cases followed dilatation of a urethral stricture, 2 followed inflammation of the prostate and vesiculae seminales, in 7 the origin was undetermined, 2 were said to have followed a squeeze. In 11 staphylococci were found, in 1 streptococci, and in 2 colon bacilli. The non-gonorrhoeal origin put forward by Kroll in the title of his communication is not substantiated by the description of his cases. By epididymectomy extension to the testis was avoided and tuberculous disease excluded by the subsequent examination. In one case only, viz. that due to streptococci, had the infection extended beyond the epididymis to the testis.

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W. G. S.

THE OPENING OF DEEP-SEATED ABSCESSES FOLLOWING GUNSHOT WOUNDS OF THE ABDOMEN FROM BEHIND THE PERITONEUM

Pribram had had occasion to operate upon 170 cases 24 hours to 4 weeks after gunshot wounds of the abdomen, and in those in which there was deep-seated suppuration after the lapse of two or three weeks he found it advisable to approach the site of the suppuration from behind. Intraperitoneal faecal abscesses are enclosed in adhesions, and a patient may in the course of weeks or months waste and die without the seat of the suppuration being diagnosed. The signs are likely to be indefinite, the most constant symptom being an evening rise of temperature, with some diarrhoea. It must be taken as exceptional for such an intraperitoneal abscess, enclosed by adhesions, to subside spontaneously by opening into the intestines. A consideration of the nature of the course of the bullet, assisted by an X-ray examination, may lead up to the locating of the abscess. Then the abscess may be reached from behind without disturbing the adhesions which shut off the suppuration from the rest of the abdominal cavity. On the other hand, a free laparotomy and the examination of the gastro-intestinal canal soon after adhesions have formed is almost certainly fatal.

An abscess in the upper part of the abdomen may be reached from behind and be found to be subphrenic in position, or situated in the lesser peritoneal cavity, or in the region of the hepatic or splenic flexure of the colon. When the abscess can be opened from the loin, even if it communicates with the ascending or descending colon, the perforation may close spontaneously. An iliac abscess may be found limited behind by the venter ilii and in front by the caecum or sigmoid flexure; it may then be drained through a notch cut in the ilium. The suppuration may take the course of a psoas abscess and pass under Poupart's ligament into the thigh, or through the great sciatic notch into the buttock, or, tracking into the pelvis, it may be exposed by exploring beside the rectum. An intraperitoneal operation for an abscess which has followed a wound of the rectum is most unsatisfactory; the best approach is from below and behind, after excision of the coccyx or in addition of the lower end of the sacrum.

The most difficult is an abscess between coils of the small intestine; generally speaking, the first operation should be limited to evacuation of the pus without destroying adhesions. At a subsequent operation it may be found practicable to close a faecal fistula without opening the general peritoneal cavity.

Case I. A man was wounded, in July 1916, by a bullet which entered the middle line of the abdomen, 3 fingers' breadth under the xiphoid cartilage, and made exit through the left loin. For 7 days he was kept short of food, but vomited even after drinking water. Twenty days after he felt well and was taking a light diet. Twenty-five days after there was sudden collapse followed by death. In the peritoneal cavity on the left side were adhesions, in the pelvis old blood-clot, in the lesser peritoneal cavity faecal extravasation and pus, in the posterior wall of the stomach a hole the size of a crown-piece, in the transverse colon two holes the size of farthings.

Case II. A man was wounded soon after the above, the bullet entering to the inner side of the right anterior superior spine, and making exit through the left loin. There was only slight pain in the ileo-caecal region when, after being on a light diet, on the 10th day he had sudden pain and a rapid pulse, the abdomen continuing soft and the tongue moist. An incision through the wound of entry reached stinking pus and faeces in a loculus of the peritoneum, in which was necrosed omentum and a hole into the caecum the size of a farthing. The gangrenous omentum was removed and a counter-opening made in the right loin. An incision was then made through the wound of exit and a faecal abscess opened behind and around the sigmoid flexure. Both incisions were drained, colon faeces escaped on the right side and small intestine faeces on the left. At a second operation on the left side two holes into the small intestine were closed, the opening into the caecum on the right closed spontaneously five weeks from the injury, and he was discharged healed.

Case III. The wound of entry was two fingers' breadth under the xiphoid cartilage; the wound of exit was through the right intercostal space, a hand's breadth from the middle line behind. There were no marked symptoms but T. 38·5° C., cachexia, and rapid wasting. A left-sided subphrenic abscess was noted by X-rays, and this was drained by removing the 6th rib. The man died, when faeces and pus were found in the lesser peritoneal cavity with two holes into the duodenum. It had been shut off by the liver from the subphrenic abscess, which had been drained.

Case IV. A Turk had a wound of entry through the right loin, and that of exit in the left hypochondrium. At first there was little disturbance; after three weeks wasting commenced, and the X-rays seemed to show an abscess in the lesser peritoneal cavity. So, 27 days after the injury, an incision was made and the 12th rib on the left side removed. Through this a deep abscess containing foul pus was reached, from which bile escaped, also milk soon after it had been swallowed. Rapid wasting to a skeleton ensued; at a second operation, seven days after the first, jejunostomy was established and improvement followed. At a third operation, a week after the second, the pylorus was excluded and gastrojejunostomy performed. Further improvement followed feeding by mouth. At a further operation, two months after the wounding, the duodenal fistula and the jejunostomy opening were both closed. Six weeks later the patient was discharged healed.

Keppich described the case of a man aged 22, who had a gunshot wound of the rectum, which was sutured at once, also the abdominal wall was closed. Three weeks later there was suppuration, he was much wasted, T. 38·3° C., P. 112. The wound of entry was 3 cm. to the right and just above the level of the umbilicus; the wound of exit was in the outer half of the left buttock, about the middle of the ilium. Both wounds were dilated, but there followed signs of deep suppuration. Therefore, 23 days after the injury, an oblique incision was made behind the peritoneum in the left loin, which exposed the ureter and back of the descending colon, and then the common iliac artery and vein. An abscess was thus reached and 100 c.cm. of pus let out, also a hole through the ilium was dilated and drained. Subsequently two abscesses were opened in the buttock. The man healed in six months, and a year after the wounding was quite well.

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W. G. S.

TOPICAL TREATMENT OF LARYNGEAL TUBERCULOSIS

Cases of primary tuberculosis of the larynx are a vanishing quantity owing to the more thorough examination of the pulmonary apices, especially by means of the X-rays. At very early stages of such tuberculous disease, and in a large number of the cases, there is an extension to the larynx by way of blood-vessels and lymphatics. Laryngeal tuberculosis in its early stages is benefited in the same way and to the same degree as early pulmonary tuberculosis by the sunshine and dry air at a high altitude of a mountain climate, when the residence there is prolonged. The progress of the disease is slow, extending over seven years or more, and there is a lack of evidence that any purely local treatment affords more than temporary relief. It follows that the local application of light such as X-rays to the outer aspect of the larynx, or the reflection of sunlight or other light to the larynx by means of a mirror is not likely to make a real advance. The following communications aim at the simultaneous exposure to the light of the apices of the lungs and of the larynx.

The gist of a long serial paper by Blegvad is the claim that by a combination of universal carbon-arc light treatment with local treatment, consisting mainly of deep puncture with the galvano-cautery, better results can be achieved than by any method previously advocated. This claim is the more interesting as Blegvad's countryman, Professor Saugman, speaking of his experiences at Vejlefjord Sanatorium, recently maintained that the most effective treatment of laryngeal tuberculosis was the sanatorium régime which aims at arresting pulmonary disease and restoring the patient's general vitality. For the past 2½ years Blegvad has been treating laryngeal tuberculosis at the Öresund's hospital with powerful carbon-arc lamps (20 ampère). The patient, being stripped and recumbent, the whole body is exposed to this light. The exposures are given daily, the duration of each being 15 minutes for the first week, and are increased by 15 minutes every week up to the fourth week, when each exposure lasts an hour. Owing to lack of accommodation the treatment was not always continued as long as desirable, and for the same reason many of the patients returned to their homes after each treatment.

Of the total of 74 patients, most of whom belonged to Turban's third stage of pulmonary tuberculosis, 14 achieved complete arrest of their laryngeal disease, and 3 showed only slight redness of the lining of the larynx. There were also 35 patients whose laryngeal disease showed definite improvement. Six showed no improvement, and in 16 cases the disease was progressive in spite of the treatment. It has become almost a dogma that laryngeal disease runs a course parallel with that of the lungs. Blegvad does not accept this as a general rule. In many of his cases the disease of the larynx became worse, while that of the lungs became better; and in several cases the reverse was observed. Accordingly, he advocates local as well as general treatment, and he emphasizes the need of skilled laryngological supervision. The force of his advocacy of universal carbon-arc light treatment is somewhat weakened by his admission that the results of this treatment were much improved after he began to supplement it with local applications of the galvano-cautery. Combined, these two methods have been so effective that he has seldom had to resort to morphin and cocain or injections of alcohol into the superior laryngeal nerve to relieve dysphagia.

Strandberg has treated 18 cases of tuberculosis of the larynx at the Finsen Institute, in Copenhagen, with carbon-arc or quartz-mercury lamps. After excluding 5 cases, in which the treatment was discontinued too early for any definite benefit to be obtained, he discusses the subsequent fate of the remainder. Nine were apparently cured, and in 2 of these cases the cure had been maintained for almost 3 years. In 6 of these 9 cases there had been no local treatment, and the results were due to the actinotherapy alone or to a combination of this treatment with ordinary sanatorium treatment. Strandberg finds that the arc-lamp is probably superior to quartz-mercury light. This is, however, to be preferred when the heat generated by the arc-lamp embarrasses the patient. Using the arc-lamp, he usually begins with an exposure of 20 minutes, and he increases this gradually to about 2 or 2½ hours. He uses 3 lamps at a time, of 20 ampères each. The exposures are given every other day, the patient is recumbent, and the whole body is exposed. Strandberg concludes that this treatment is an important advance as far as laryngeal disease is concerned.

Begtrup-Hansen has adopted actinotherapy at Silkeborg Sanatorium since 1914, and he has treated 146 cases of pulmonary and surgical tuberculosis with quartz-mercury light. He tabulates his results, which he considers, on the whole, to be good. After commenting on the difficulties experienced in distinguishing between the good effects of actinotherapy plus sanatorium treatment and those of sanatorium treatment alone, he confesses to depending more on general impressions than on figures. In about 40 cases the actinotherapy probably played an important part in the improvement effected. Pleurisy, in particular, responded with striking effect; and it appeared that the more superficial the disease, the more effective was its response to this treatment. His material included 28 cases of laryngeal tuberculosis, in 22 of which definite infiltration and ulceration were present. All the 6 slight cases cleared up under actinotherapy, and of the 22 advanced cases, 6 were cured, 8 were improved, 5 were stationary, and 3 became worse. Begtrup-Hansen's impressions as to the response of laryngeal tuberculosis to actinotherapy are favourable; this disease reacts more satisfactorily than pulmonary tuberculosis, but less satisfactorily than surgical tuberculosis to actinotherapy. He insists on the treatment being continued for a long time; most of his patients received between 100 and 200 exposures, and some received as many as 400.

Holmboe's verdict on actinotherapy is guarded, but on the whole favourable. By itself it is no panacea; but in sluggish cases failing to respond satisfactorily to sanatorium treatment, actinotherapy gives a fillip which starts the patient in the right direction. Holmboe publishes some interesting figures, showing the effect of actinotherapy on haemoptysis. Between 1909 and 1915, when he relied on sanatorium treatment alone, the incidence of haemoptysis varied from year to year between 12·6 and 16·4 per cent. During the first 3 years of actinotherapy the incidence of haemoptysis was 5·3 per cent., 2·1 per cent., and, in the third year, only 1·9 per cent. He correlates this striking decline with the introduction and increasing practice of actinotherapy, and he suggests that the cutaneous hyperaemia provoked by actinotherapy may induce a fall of blood-pressure in the lungs. This hypothesis is the more plausible as the hyperaemia of the skin resulting from actinotherapy may continue several months after this treatment has been discontinued.

A curious and a somewhat paradoxical observation is made by Malmström, who, since February 1914, has treated about 400 cases, chiefly pulmonary and laryngeal tuberculosis, with sunlight and the quartz-mercury lamp. He achieved as great a proportion of successes among his sputum-positive as among his sputum-negative cases, and improvement was effected in 44 per cent. of his febrile cases, and only in 35 per cent. of his afebrile cases. He also found that in surgical tuberculosis his results were often better when the glands were enormously swollen and suppurating than when the tuberculous adenitis was slight and early. He makes no attempt to interpret this anomalous state of affairs. Though in 43 out of 306 cases of pulmonary tuberculosis the actinotherapy provoked a reaction, such as is sometimes observed when tuberculin is given, he has never seen permanent ill effects from this treatment. He is not hotly enthusiastic over actinotherapy in pulmonary tuberculosis, but he is sufficiently impressed to continue this treatment and to recommend it to others. He notes as significant the fact that the proportion of positive results increases greatly with the number of exposures; his results were much better among the patients who were given 60 or more exposures than among those who received fewer than 60 exposures.

Reyn's advocacy of actinotherapy in pulmonary tuberculosis is a reflection of the dramatic results he has observed in cases of surgical tuberculosis and lupus at the Finsen Institute. He follows up this *a priori* line of argument with several practical hints as to technique and choice of lamps and cases. He uses 20 as well as 75 ampère lamps, and he gets over the difficulty of the embarrassing heat of the powerful carbon-arc lamps by the simple expedient of increasing the distance between them and the patient. He has found the carbon-arc lamp greatly superior to the quartz-mercury lamp, the chief advantages of which, in comparison with the carbon-arc lamp, are its entailing less fatigue for the patient, and its generation of less heat. It has, therefore, a certain sphere of usefulness in cases of general debility, and it may be employed with benefit when, at the beginning of treatment, the carbon-arc lamp is apt to provoke too violent and exhausting a reaction. It appears from these publications that in the Scandinavian countries actinotherapy in pulmonary tuberculosis has come to the fore, and bids fair to rank with sanatorium treatment and lung collapse in popularity.

Two methods of surgical treatment give relief, not to the disease, but to a complication, laryngeal obstruction. If at an early stage marked oedema appears and the galvano-cautery point is plunged deeply into the most prominent place, at one spot, an inflammatory reaction supervenes, followed by shrinkage. No more than one puncture at a time is made in the case of an out-patient for fear of oedema glottidis. If a tuberculous nodule, a so-called tuberculoma, or swollen mass of mucous membrane and submucous tissue obstructs breathing, it is removed by cutting forceps or a snare through the mouth. A procedure of very doubtful expediency is that of curetting an ulcer followed by the application of concentrated lactic acid, &c. At this stage the pulmonary disease is no longer in its earliest stage and the curetting is likely to be followed by an exacerbation.

In the later stages of the disease good relief can be given; pain and dysphagia are removed by cutting out the superior laryngeal nerve on both sides. In 1908 Hoffmann introduced the injection of 80 per cent. alcohol into the nerve before it penetrates the thyroid membrane. Cases have been so relieved even for months, generally for only a shorter period; but the nerve is often missed. Hence Avellis in 1909 proposed the division of the nerve as more thoroughgoing.

Wachmann, of Bucharest, reported in 1916 five cases, the operation being performed after the injection of novocain. A horizontal incision is made between the hyoid bone and the thyroid cartilage, the platysma and deep fascia are divided; the omohyoid and sternothyroid muscles are retracted towards the middle line; the fibres of the thyrohyoid are exposed, also the superior laryngeal nerve with its accompanying artery just before it penetrates the membrane. The nerve is hooked up just behind the outer edge of the thyrohyoid muscle, between the lower margin of the middle and the upper border of the inferior constrictor, and a length excised. The five cases, previously suffering from severe dysphagia, were immediately relieved, and could take a variety of food.

Zencker, reporting on the results of the operation, held that it is indicated in order to give relief to a patient soon to die; in earlier cases it definitely aids the healing of an ulceration.

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THE ORIGIN AND NATURE OF THE EXTENSOR PLANTAR RESPONSE: BABINSKI'S TOE PHENOMENON

Historical. Perhaps no single physical sign has a more definite clinical significance or is of greater importance than Babinski's 'phénomène des orteils', the extensor plantar response of English writers. There is no field of clinical neurology that has not been enriched by the genius of Babinski, but probably none of his contributions to our knowledge exceeds in value his discovery, in 1898, of this reflex and his demonstration that it indicates disordered function of the pyramidal system of fibres and this alone. Since that time it has been the subject of much speculation, yet until within the past eight years its origin and physiological significance remained totally unsuspected. This was not surprising, for writers did not base their theories upon careful examination or analysis of the reflex itself, but, content to gaze upon the upturned great toe, they almost unanimously conceived the idea of invoking the theory of evolution to explain the phenomenon. Hypotheses based entirely upon phylogenetic considerations have always possessed a peculiar fascination for neurologists, more particularly in other countries than our own. For although such hypotheses must of necessity remain for ever speculative, yet they possess the redeeming charm of being incapable of disproof. Wherever in clinical neurology we find the lessons of the experimental physiology of the nervous system neglected, or unable to assist us, there we find speculation of this order most abundant and most extravagant. With the disciples of this school, a familiar mode of explaining an obscure clinical phenomenon is to adopt the figment of 'a primitive animal' and to endow it deliberately with a nervous system so ill-adapted and so defective as inevitably to entail the early extinction of its possessor. From so tragic a fate, however, this impossible creature of the imagination is always saved by some timely and predetermined addition in its creator's hypothesis, which is thereby justified. Thus, in a recent paper of this type, only the happy thought of the author in creating a special 'inhibitory tremor centre', in that safe hiding-place the subthalamic region, saved his 'primitive animal', and, more terrifying still, man, its descendant, from being for ever addicted to a Parkinsonian tremor. This being so, it must have been easy to foretell the view that would be taken of the extensor plantar response. It was at once said to signify a reversion to the prehensile functions of the great toe of our 'arboreal ancestors'. So striking an atavistic phenomenon could not fail to stimulate the imagination, and in fact the 'prehensile toe' has become a veritable 'Will-o'-the-wisp', beckoning to us out of the pages of many earnest monographs and papers. As might have been expected, it has not led its followers upon the path of knowledge.

During this speculative era, then, nothing was added to our knowledge of the origin or nature of the reflex, though indeed a certain amount of clinical information was obtained. It was found by various observers that under similar conditions of pyramidal tract disease the same reflex movement of the hallux could be elicited by other forms of stimulus than that which was employed by Babinski, namely, stroking the sole. Thus, pressure over certain bones, tendons, and muscles in the region of the foot and ankle were found to give an extensor response. It was not realized that the areas and structures thus stimulated were but parts included within the receptive field of a single reflex movement. In consequence, a custom sprang up, happily not in this country, of testing the plantar response by all these methods and of recording the results clinically in the form of a list of the names of their discoverers. Thus, in a case of nervous disease giving a normal plantar response we may read 'Babinski, Oppenheim, Gordon, Chaddock, Redlich, Rossolime, Schaefer, and Mendel-Bechterew negative'. The neurologist of a future and more rational generation will probably be puzzled to decide whether these names record the votes of the individuals mentioned upon some moot point of neurology, or whether they refer to biochemical tests, or what not.

Modern study of the reflex. The serious investigation of the reflex was first undertaken by Pierre Marie and Foix in 1912. Studying in cases of paraplegia the well-known flexor spasms, which occur spontaneously and on stimulation in the region of the foot (Babinski's 'réflexes dits de défense', 'Abwehrbeugereflexe' of German writers), these observers came to the conclusion that the general movement of withdrawal or flexion of the limb, of which these reflexes consisted, included as an integral part the extensor plantar response, and further that this plantar response was the minimal manifestation of such reflex flexion. Finally, they observed the occasional occurrence of reflex extension of the opposite limb in association with reflex flexion, and they concluded that these phenomena were analogous with the 'reflex stepping' of the spinal animal. They called them 'réflexes d'automatisme médullaire', since they were seen only when the cord was released from higher nervous control by lesions severing descending paths. This interpretation was questioned by Babinski and Déjerine, both holding that the extensor plantar response was a distinct and separable reflex, and both objecting to Marie and Foix's phrase 'réflexes d'automatisme médullaire'. The arguments employed by these authorities have proved illusory and have been dealt with in a paper to be mentioned later. Although Marie and Foix's view has required certain modifications, yet there can be no doubt that it was a distinct advance upon earlier hypotheses and helped to place the study of the reflex phenomena of spastic paralysis of the lower limbs upon a scientific basis.

In a paper published in 1914, Walshe gave the results of a study which was based upon the desire to correlate as far as possible the various reflex phenomena of spastic paralysis and to determine whether those principles of the co-ordination of movements found to obtain in animals by Sherrington were applicable to man. He studied the extended and flexed form of spastic paraplegia, and also, within narrower limits, the flaccid paraplegia of total physiological transections of the cord. Among the conclusions reached were the following: (1) that the reflex movements of the lower limbs in spastic paralysis are almost entirely movements of flexion. With flexion is included dorsiflexion of foot and toes, more especially the great toe. Although the dorsiflexors are known in anatomical nomenclature as extensors there are convincing reasons for regarding them from the physiological point of view as flexors. The reflex movements of flexion occur in the well-known flexor spasms of paraplegia, and also on appropriate stimulation of the limb. This form of reflex movement may be called the '*flexion reflex*' (adopting Sherrington's nomenclature). (2) The 'receptive field' of this reflex may include the whole limb, skin, and deep structures, except for a small portion of the proximal part. The reflex, therefore, is not purely cutaneous. The form of stimulus most effective is one having a nocuous or harmful character, but light painless stimuli applied to the distal extremity of the limb (the sole) suffice to evoke the reflex. The muscles actuated are the limb flexors and the reflex response is a simple flexion at all joints. (3) *Of this reflex flexion, dorsiflexion of the hallux is an integral and inseparable part and constitutes the extensor plantar response,* Babinski's 'phénomène des orteils'. The extensor response is therefore part of the flexion reflex, and never occurs without discoverable contraction of proximal limb flexors (e. g. the hamstring muscles). (4) The physiological significance of the flexion reflex, and therefore of its component the extensor plantar response, is that of a defensive reflex, *Sherrington's 'nociceptive flexion reflex'*, and it has no relation to 'spinal stepping'. Marie and Foix failed to note the fact that reflex stepping is a proprioceptive reflex induced by passive movement of the limb and not by cutaneous or nocuous stimuli. Moreover, the work of Riddoch, to be referred to later, has shown that the flexion reflex is obtainable after total transection of the cord, when reflex stepping cannot be induced. (5) The contraction of the limb flexors in the flexion reflex is accompanied by reciprocal inhibition of their antagonists in the same limb, the extensors and plantar flexors. (6) Accessory to this reflex is the crossed extension reflex in the other leg, which includes plantar flexion of the foot and hallux, the '*crossed plantar reflex*' of Bramwell and others.

Flexor and dorsiflexor muscles. Possibly the statement that the dorsiflexors are to be considered as physiological flexors and not as extensors needs some amplification. Sherrington has shown in animals, and Beevor has confirmed the observation in man, that muscles regarded as anatomical units are not always employed so. Thus quadriceps extensor femoris physiologically considered is two muscles; rectus femoris, which acts as a flexor of the hip and has nothing to do with the knee-jerk; and the vasti, which are purely knee extensors and are the muscles of the knee-jerk. Moreover, muscles acting over two joints, such as quadriceps or the hamstrings, are not employed by the co-ordinating mechanisms of the nervous system to produce movement at both joints. Thus Sherrington has shown that biceps femoris is so placed as to be able to act as an extensor of the hip and as a flexor of the knee. In normal co-ordination it is employed solely as a knee flexor, its action upon the hip being countered by contraction of the hip flexors, which here act not as antagonists to the biceps, but as synergic muscles ('pseudantagonists'). Therefore, enough has been said to indicate that anatomical nomenclature is by no means a guide to function. The position of the dorsiflexors is, however, not quite met by the examples given above, and their claim to be regarded as flexors rests upon other but equally cogent grounds. Sherrington has shown that in the hind limb of the spinal animal, which like that of man is primarily a locomotor organ and prop, the dorsiflexors act with the flexors in movements having alternate flexion and extension phases, and that they act with the flexors in the flexion reflex. Conversely, the plantar flexors act with the extensors in the rhythm of stepping and of the scratch reflex, and in the simple extensor thrust and crossed extension reflexes. Further, the plantar flexors exhibit that postural tonus so characteristic of extensor or 'anti-gravity' muscles, while their antagonists the dorsiflexors do not. Finally, just as dorsiflexors and flexors contract together, so in reflex movements of the limb they are inhibited together by reciprocal innervation. There can be no reasonable objection, therefore, to the view associating flexors and dorsiflexors physiologically, though it involves a departure from an anatomical tradition. Sherrington and Beevor have clearly demonstrated that although mechanical factors are of importance in the motor co-ordination of the organism, we cannot determine the functions of muscles solely from the study of their attachments and the leverage which this allows them to exert on joints.

Although there was no doubt of the purely spinal origin of the flexion reflex in the experimental animals of Sherrington, the results of spinal transection in man were at the time believed to differ so completely from those found in the lower animals under similar conditions, that a demonstration of the extensor response in a 'spinal' man was necessary to establish a complete analogy between man and the lower animals. Bastian had taught that after complete division of the cord in man there followed a flaccid palsy with complete loss of all reflexes in the lower limbs. Later, Collier found that 'certain skin reflexes', by which he meant contraction of some of the thigh muscles on cutaneous stimulation, persisted in these circumstances. In three cases of complete flaccid paraplegia following cord lesions, which were regarded as physiologically complete transections of the cord, Walshe found that minimal traces of the flexion reflex remained and consisted of an extensor plantar response and a palpable contraction of the hamstring muscles accompanying it. Therefore, his observations indicate that the extensor plantar response is a spinal reflex movement appearing when cerebral control over spinal reflex arcs is removed by impaired activity of the pyramidal system of fibres (either by structural disease or by transient inactivity as after an epileptic convulsion). It is most readily elicited from the distal extremity of the limb, the sole of the foot, but usually it is also obtainable by a variety of nocuous stimuli to bones, tendons, muscles, and skin of almost any part of the limb. It is part of a general reflex flexion of the lower limb, protective in its original purpose, and usually some trace of this general flexion is readily apparent. A crossed plantar response of plantar flexor type may accompany it, and is a manifestation of reflex extension of the opposite limb.

The plantar response in total transection of the cord. The study of the reflexes in clean division of the spinal cord by gunshot wounds has not only confirmed this view of the origin and nature of the extensor response, but has thrown much additional light upon the functions of the spinal cord. Many aspects of this recently acquired knowledge are beyond the scope of the present review and will be dealt with in a forthcoming number of *Medical Science* by Dr. G. Riddoch. However, the condition of the plantar response in these circumstances is of primary interest in the present connexion.

In the first two years of the war, the experience of Gordon Holmes, Collier, Guillain and Barré, Déjerine and Mouzon, and other French observers seemed to indicate that the extensor plantar reflex disappeared after total transections of the cord. Guillain and Barré studied sixteen cases of verified division of the cord and found that the plantar reflex retained its plantar flexor type, but differed from the reflex of the normal subject in its long latent period and in the slowness of the reflex movement. Accompanying it they observed in several cases contractions of leg and thigh muscles, but the significance of this observation appears to have escaped them. Déjerine and

Mouzon stated that 'la réaction à l'excitation de la plante du pied se traduit habituellement par la flexion plantaire du gros orteil'.

It is clear now that all these observers studied their cases only in the stage of spinal shock that immediately follows division of the cord, and from which many cases never emerge. Further, the complicating effects of bed-sores and cystitis and general septic infection had in many instances still further depressed the reflex activity of the isolated cord.

Riddoch (1917), in the course of a careful investigation and analysis of eight cases of total cord transection, established quite clearly that the flexion reflex with the extensor plantar response, which is a part of it, not only appears after division of the cord, but becomes a remarkably active and dominating feature of the clinical picture. His observations may be briefly summarized as follows. Following total transection of the cord the isolated segments enter into an *initial phase of spinal shock*. Under favourable conditions of nursing of the patient (the prevention of bed-sores and cystitis) the isolated portion of the cord emerges gradually from shock after two or three weeks and enters *a second phase, that of reflex activity*.

During the initial phase there is, as Bastian originally taught, a flaccid paraplegia with loss of tendon and plantar reflexes. The anal and bulbo-cavernosus reflexes alone remain. The phase of reflex activity opens when, in response to stimulation of the skin or deep structures of the lower limb, a reflex contraction of the limb muscles is obtained. The first muscles to respond are the limb flexors and the necessary stimulus is one of nocuous character, applied to the sole of the foot. The initial motor response may be an extensor plantar response, but in some cases the appearance of this is preceded by the plantar flexion movement described earlier. This downward movement of the toe does not persist for any length of time, and is soon replaced by a *definite extensor response*. As reflex activity returns, the receptive field and the motor response both increase in extent until a full flexion reflex can be obtained from the whole limb, and even in some cases from the abdominal wall. Riddoch also found that where the initial plantar flexor response was seen, it sometimes persisted after the development of reflex flexion at the proximal joints, so that stimulation of the limb evoked hallux plantar flexion and limb flexion. However, Riddoch noted that this plantar flexion preceded and did not synchronize with the limb flexion, and was in one case followed by an extensor response, as Walshe had earlier found in spastic cases. From which we may conclude that the plantar flexion is no part of the general flexion reflex, but a distinct reflex which is not yet explained. In conclusion, Riddoch confirmed the view that the extensor response was an integral part of the spinal nociceptive flexion reflex, and showed further that this reflex is at once the earliest to emerge from spinal shock, and the most prominent reflex act of the isolated spinal cord when this has regained full reflex activity.

From what has been said of the nature and significance of the extensor plantar response, it will be seen that it is part of a reflex using the flexor muscles of the limb, and it is not a reflex.contraction of true extensor muscles. It is unfortunate that a purely anatomical nomenclature should have necessitated so paradoxical and confusing a state of affairs. Undoubtedly, the council of perfection in this matter would be to speak of the extensor response as the flexion reflex, and to refer always to the normal so-called flexor response as the normal plantar reflex. Unfortunately, the clinical terms at present in use are so firmly planted in the neurological literature of this country that their replacement is hardly likely. Perhaps a way out would be to speak of 'Babinski's toe phenomenon' or the Babinski response, for although, as we have seen, the literature on the reflexes is greatly overloaded with irrelevant names, Babinski's fundamental contribution to clinical neurology in the discovery of this reflex might not unreasonably be honoured thus, in this country, as it is elsewhere.

The normal plantar reflex. Although the clinical investigations we have reviewed, carried out largely under the inspiration of Sherrington's physiological researches, have added to our knowledge of the reflex phenomena of spastic paralysis of the lower limbs and to that of the functions of the isolated cord in man, yet many aspects of these problems remain obscure. One of these is the relationship, if any exist, between the normal plantar reflex and the extensor plantar response. In pyramidal tract lesions the tendon reflexes are increased in activity while all purely cutaneous reflexes are abolished. There is reason for regarding the *normal plantar reflex* as one of the cutaneous reflexes which disappear in this way. It seems to be purely cutaneous. It is best elicited by light, painless stimulation of the sole, and has a small receptive field limited to the sole. The motor response includes plantar flexion of the hallux and sometimes plantar flexion and adduction of all the toes. Tensor fasciae femoris is also included among the muscles constantly involved, as Brissaud was the first to emphasize. If we employ rough or painful stimulation the motor response appears to spread widely, but not in any constant fashion. Muscles contract which are not synergically related; sometimes the limb is stiffened in extension, sometimes it is flexed, while not rarely a rapid ample dorsiflexion of the hallux may replace the plantar flexion movement of the true reflex. It is clear that in these circumstances the true reflex response is complicated by the presence of voluntary movement, and is thus rendered extremely difficult of examination and analysis. The plantar muscles and tensor fasciae femoris, the normal motor field of the reflex, derive their innervation from the first sacral segment of the cord, and it has therefore been said that the normal plantar reflex is a unisegmental cutaneous reflex. However, some observations of uncertain significance made by Graham Brown and Stewart suggest the possibility that the normal plantar reflex may not be purely cutaneous and may have a receptive field wider than the sole. Further investigation on this point is needed to clear up the element of uncertainty that still exists as to the characters of this reflex.

It has been stated earlier that occasionally a plantar flexion movement of the hallux is seen accompanying the reflex flexion of the proximal joints in spastic conditions. A case showing this combination has been quoted by Babinski and by Déjerine as evidence that the flexion reflex and the extensor response are distinct and separable reflexes. Their case, however, is of no value in this connexion, for reference to Déjerine's original clinical report of the case shows that the hallux was fixed by 'rétractions fibro-musculaires' and therefore could not possibly dorsiflex. Moreover, we have seen that this plantar flexion usually precedes and does not accompany the limb flexion, and that it may be followed by a dorsiflexion movement of the great toe (diphasic toe movement) which is synchronous with the limb flexion. This is equally true of spastic cases and of the early plantar flexion reflex of the isolated cord in spinal shock. Both Gordon Holmes and Guillain and Barré have recorded that the normal plantar reflex differs in some of its features from this early plantar flexion reflex of 'spinal' man, and the exact relationship of these two reflexes has yet to be elucidated. There seems little doubt, however, that both are quite distinct from the flexion reflex we have been studying. In the case of the normal plantar reflex the recognition of this difference in adequate stimulus, receptive field, and motor reaction from the corresponding features of the extensor response is of importance. For, if the significance of the latter is what we have stated it to be, then it would seem to be an example of a purposive reflex of great value that the normal nervous system none the less does not employ, for no such reflex can be demonstrated in the intact individual. It might appear unreasonable, therefore, to call a reflex movement which occurs only under conditions of disease a protective reaction. Such an objection might possibly arise from the assumption that the normal plantar reflex fills the place in the normal state that the flexion reflex with its component extensor response fills in the abnormal, and that this normal reflex is the true protective one. There is no ground for such an assumption. As we have indicated, the two reflexes appear to present certain fundamental differences and cannot readily be compared in the present state of our knowledge. We have as yet no clear conception of the functional significance of the normal reflex, and therefore the theory of the origin and meaning of the extensor plantar response should be judged on its merits and not in relation with the normal reflex.

We must also take into consideration the influence of the cerebral cortex on the reflex levels of the nervous system. The studies of Head and of Sherrington upon the functions of the sensory and motor cortex respectively have indicated that the cerebral cortex exerts a discriminative control of the greatest possible refinement upon lower level mechanisms. The statement is often made that it inhibits the activity of the spinal reflex arcs. To say this is to state but a fragment of the truth. The cerebral centres exert control over the activity of these arcs and over all lower level arcs and can inhibit or excite most of these to any degree or to any extent. It is very characteristic of this controlling action that it includes the selection and combination into large purposive movement complexes of the various constituent elements of the simpler reflex movements carried out by these lower level arcs, and the inhibition of conflicting elements in these movements. In the cerebral cortex of man this discriminative and analytic function reaches its highest level. It is therefore scarcely surprising if in the intact individual the primitive spinal reflexes are profoundly modified and rarely recognizable. Even in the lower animals in their normal state we cannot readily or certainly elicit the various reflex phenomena that have been so extensively studied in the decerebrate and spinal preparations. Yet some of these reflexes, such as the scratch reflex and reflex stepping, are so eloquent of purpose that we cannot deny that they are purposive reactions, even though we are unable to obtain them in the intact animal at will. The apparent submergence of a reflex, such as the extensor plantar response, when the cerebral cortex is in full control of the motor machinery is not necessarily an argument against the view of its meaning that we have taken here.

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F. M. R. W.

ABSTRACTS

SURGERY

NICOLAYSEN, N. A. Erfaringer med Carrel-Dakin's saarbehandling. [**Carrel-Dakin's treatment of wounds.**] *Norsk Mag. f. Lægevidensk.*, 1920, **81**, 786–803.

Nicolaysen's verdict as to the efficacy of Carrel-Dakin's treatment is not unreservedly favourable. The first 36 patients treated by this method at the Communal Hospital in Bergen included cases of compound fracture, extensive lesions of the soft tissues, pyarthrosis, osteomyelitis, empyema, and one case of acute tendo-vaginitis. Disappointing results from a bacteriological point of view were obtained in the five cases of extensive lesions of the soft tissues. In three of these cases this treatment was not instituted till some time after the injuries were inflicted, and it effected definite clinical improvement. But in no case could sterility of the wounds be achieved, and in a case of pyocyaneus infection the sterilizing effect of the solution was practically negligible. Similar results were obtained with the four cases of osteomyelitis; the clinical results were good, but even approximate sterility was not obtained. As for the 15 cases of empyema, there were three in which an attempt was made to sterilize large cavities and to close them early. The immediate effects were striking: suppuration practically ceased, smell vanished, and the number of micro-organisms was much reduced. But soon after removal of the drain and closure of the wound, reinfection occurred, necessitating renewed drainage. The less ambitious application of this treatment to the later stages of empyema proved far more satisfactory, and the irrigation of short fistulae and small cavities with the *C–D* solution did much to hasten recovery. Although this treatment was adopted early in a case of acute suppurative tendo-vaginitis, the results were very unsatisfactory. In none of his cases of compound fracture did N. succeed in reducing the number of micro-organisms to the level demanded by Carrel and Dehelly. One of N.'s most instructive cases was that of a man on whom prostatectomy had been performed. Irrigation of the bladder with the *C–D* solution caused no burning or other sensation, but 20 minutes later a rigor developed with hyperpyrexia. The treatment was discontinued accordingly. Scattered throughout N.'s paper are suggestions that the treatment may not only fail, but be actually injurious; he thinks his failures with pyarthroses may possibly be traced to the action of the solution on the synovial membranes. C. L.

SUNDT, H. Meddelelse fra Kysthospitalet ved Fredriksvern. [**Report from the Fredriksvern Hospital for scrofula and surgical tuberculosis.**] *Med. Rev.*, 1920, **37**, 5–30.

Sundt's paper shows that with modern diagnostic methods it is possible to sort out as non-tuberculous more than 43 per cent. of all cases diagnosed as tuberculosis of the hip by ordinary clinical examination. On the approach of the 25-year jubilee of his hospital, S. set himself the task of tracing the patients discharged in this period with a view to finding out how many had contracted or died of pulmonary tuberculosis. But he soon found that so many of his cases had to be discarded as non-tuberculous, that the investigations he had planned would throw little light on the question: Does scrofula or surgical tuberculosis in childhood afford any protection against pulmonary tuberculosis in later life?

In the period August 1903–June 1918 there were 243 cases of hip disease sent to hospital as tuberculous, in 19 of which no definite diagnosis could be made. The remaining cases included the following: Coxa vara (3), epiphysiolysis coxae (2), fractura colli femoris (1), arthritis deformans coxae (15), osteomyelitis coxae (6), syphilitic? coxitis (2), non-tuberculous synovitis coxae (1), claudicatio hysterica (1), Calvé-Perthes disease (41), coxitis tuberculosa (171). Thus, 29·6 per cent. proved to be non-tuberculous. In the period July 1911–June 1918, 113 patients were admitted with the diagnosis of tuberculous hip disease. In 11 cases only such symptomatic diagnoses as 'coxalgia' and 'claudicatio' could be made. With the help of tuberculin tests, X-ray examinations, and other methods, it was found that only 64 of these 113 cases were tuberculous, i.e. 43·4 per cent. were non-tuberculous. The increased proportion of cases diagnosed as non-tuberculous since 1911 may be correlated with the introduction of v. Pirquet's test and with the growing tendency of practitioners to diagnose tuberculosis early.

S. concludes that (1) tuberculosis of the hip is considerably rarer than has generally been thought to be the case, (2) all statistics as to the results of treatment up to the present time are worthless, (3) if the benign, non-tuberculous cases could be weeded out of these statistics, the prognosis for true tuberculous disease of the hip would be found to be far worse than it was supposed to be, (4) in about 11 per cent. of all cases of hip disease it is impossible to establish an accurate diagnosis even with the help of every modern diagnostic aid. C. L.

Passow, A. Allgemeine und lokale Bestrahlung mit ultraviolettem Licht bei scrofulösen Augenleiden. [**General and local treatment of scrofulous diseases of the eyes with ultra-violet light.**] *Med. Klin.*, 1919, **15,** 1307.

Passow's advocacy of ultra-violet light in the treatment of scrofulous diseases of the eyes is enthusiastic. As Professor Hess's assistant at the University Eye Hospital in Munich, he has observed 70 cases in which Bach's quartz lamp was used. His conversion to this treatment followed the observation that when enlarged cervical glands were thus treated, coincident scrofulous diseases of the eyes cleared up promptly. Even eczematous kerato-conjunctivitis, which had proved refractory to every form of direct medicinal treatment, responded beyond all expectation to general quartz-light treatment. In most of his cases the disease was bilateral and was associated with blepharospasm, photophobia, lacrymation, and swelling of the eyelids. In more than 50 per cent. there were ulcers of the cornea, and in three cases there was hypopyon. But only in one case of hypopyon did the corneal ulceration lead to perforation during treatment. In about a third of all the cases improvement was observed after the first exposure, and in the remaining cases, with only a few exceptions, after the second or third exposure. Only in 5 cases was improvement deferred till after the third to the fifth exposure. In half the cases 1 to 3 exposures proved sufficient; in a few cases 7 to 10 exposures were required to banish signs of inflammation. Seven children required a second course of treatment owing to relapse, but 1 exposure was sufficient in these cases to restore conditions to normal.

Passow was so impressed by the efficacy of this treatment that he usually dispensed with other remedies; in a few cases he supplemented the exposures with applications of a 1 per cent. solution of silver nitrate, and at a later stage he massaged the cornea lightly with yellow ointment. The promptness with which these exposures acted was inversely proportional to the age of the child and the duration of the disease. Though he does not give figures, Passow states that the average duration of the patients' residence in hospital was appreciably shortened by this régime. In cases in which the eczematous kerato-conjunctivitis was the only symptom of scrofula, Passow dispensed with universal exposure of the body, confining the light to the eyes, which were protected from injury by the interception of the outermost, ultra-violet rays. Thus protected, the eyes were held open, and were exposed for 15 to 30 minutes at a time, at a distance of 15 cm. from a uviol lamp. Under this strictly local treatment, corneal infiltration, even when it was of old standing, cleared up more rapidly and completely than under other treatment. Passow's discussion of the action of actinotherapy throws little new light on the subject; he attaches little importance to pigmentation *per se*, as he has seen definite improvement occur before the skin had reacted by pigmentation. He sees in ultra-violet light an agent which stimulates the vitality of the skin and promotes the processes of oxidation and blood-formation. His evidence in support of these explanations seems to be mainly clinical and is otherwise meagre. C. L.

VIDFELT, G. Influensaempyemet och dets behandling. [**Influenzal empyema and its treatment.**] *Hygeia*, 1920, **82**, 545–58.

Vidfelt's study of 127 cases of influenzal empyema, treated at the Sabbatsbergs Sjukhus between October 1918 and August 1919, shows that the nature of the secondary infections greatly affected the course of the disease and its mortality. Thus, among the 70 streptococcal cases the mortality was as high as 35·7 per cent. (25 deaths), whereas among the 43 diplococcal cases the mortality was only 6·9 per cent. (3 deaths). In 7 cases there was a mixed infection and in 7 other cases the pus was sterile. Altogether the mortality for the 127 cases was 23·4 per cent. (30 deaths). The streptococcal cases were as a rule diagnosed earlier than the diplococcal cases; the former gave rise to more severe symptoms and the patients looked septic and often rapidly grew worse. In as many as 13 streptococcal cases the empyema developed during the first week of the influenza. Many of the diplococcal cases, on the other hand, began insidiously; a month or two after the onset of influenza the empyema was ushered in by moderate fever.

Reviewing the treatment adopted, Vidfelt notes that at first the streptococcal cases were treated by early thoracotomy under local anaesthesia, 5 to 10 cm. of a single rib being excised. The effect of this procedure was in some cases shock, rapid deterioration of the general condition, and death within 24 hours of the operation. The post-mortem examination of one of these cases showed total absence of pleural adhesions, the lung being completely collapsed. Accordingly the plan was adopted of repeated aspiration of the pus in most streptococcal cases, followed by irrigation of the pleural cavity. In many cases thus treated, the patient's general condition did not warrant immediate thoracotomy; but after aspiration had been repeated several times, thoracotomy could be performed without risk of serious pleural shock, as extensive pleural adhesions had formed in the interval. In 20 consecutive diplococcal cases an attempt was made to limit the treatment to aspiration supplemented by irrigation, first with normal saline solution and then with Dakin's solution. But only in 6 cases did this treatment prove adequate, and in 3 of these cases the empyema was strictly limited, and the pus did not amount to 100 c.c. In the remaining 14 cases thoracotomy had ultimately to be resorted to. In the 7 cases of sterile empyema treated by aspiration alone this proved sufficient. Of the 25 deaths, 17 occurred within the first week after operation. In no fewer than 56 cases the patients were young adults between the ages of 21 and 30. Of these 56, 22 were men and 34 were women. C. L.

NEUROLOGY

Lantuéjoul. La coagulation massive et spontanée du liquide céphalorachidien. [**Massive spontaneous coagulation of the cerebrospinal fluid with xanthochromia.**] *Rev. neurol.*, 1920, i, 339.

A review of all the recorded cases of this condition with an account of its nature and origin.

The essential features of the condition are a great increase of the coagulable protein normally found in the cerebrospinal fluid with the addition of an abnormal protein-fibrin. After lumbar puncture the fluid clots spontaneously into a firm mass within half an hour of withdrawal; in addition the fluid is always yellow tinted.

Pleocytosis is a variable and non-essential feature of this condition. Clinically, it is always found in cases of paraplegia, while pathologically the lesion giving rise to this change in the cerebrospinal fluid varies in nature. Thus, Pott's disease, syphilitic meningitis, or new growth may be the lesion found. However, whatever its pathological nature, one condition is always present and is the underlying cause; namely, a block in the spinal subarachnoid space. This is usually produced by an area of meningitis resulting in the formation of adhesions between the cord and its several membranes, or a new growth filling up the space at one or other level. The cerebrospinal fluid below the block stagnates, and is not renewed like the fluid above the block by the normal process of circulation of the fluid. It is known that there is very little absorption normally of cerebrospinal fluid from the spinal subarachnoid space. The yellow pigment always present arises from the blood pigment and is probably due to microscopic haemorrhages into the fluid in the neighbourhood of the underlying lesion. The increase of coagulable protein, both normal and abnormal, is due to transudation from the blood-vessels.

Lesions giving rise, therefore, to such a change in the cerebrospinal fluid also produce compression paraplegia. Massive coagulation with xanthochromia does not indicate the nature of the compression, but the absence of lymphocytes in the fluid is indicative of tumour or of Pott's disease of the spine as the probable cause, whereas if there are many cells a syphilitic meningitis is more probable.

The review should be consulted in the original by those interested.

F. M. R. W.

Barbé, A. Recherches expérimentales sur la perméabilité des plexus choroïdes. [**An experimental study of the permeability of the choroid plexuses.**] *Rev. neurol.*, 1920, i, 314.

Barbé has attempted to determine the physical permeability of the choroid plexuses by transfusing these structures with various fluids. The method employed consists in the removal of a plexus from the human brain at periods varying from four to forty-nine hours after death. The plexus is removed intact and is then transfused through one of its arteries, while suspended in a liquid medium.

The specimens were obtained from the brains of subjects dying from various nervous and non-nervous maladies, and the fluids transfused were tap and distilled water, cerebrospinal fluid, and serum.

He found that the plexus removed from a brain which had been fixed *in situ* by formalin injection was quite impermeable to all these fluids. From the study of this dead tissue he reaches the following conclusions: the fluid which transudes best and most rapidly is serum, transudation is earliest established and most rapid in the plexuses of young persons, persons dying from purely non-nervous diseases, and from fresh specimens; the average rate of transudation is 1 c.c. per minute, and persists for as long as twenty-four hours; certain diseases (general paralysis) increases the permeability, while others (epilepsy) diminish it. F. M. R. W.

de Lavergne. De l'altération du liquide céphalo-rachidien dans les paralysies diphtériques du voile du palais et à type polynévritique. [**Changes in the cerebrospinal fluid in diphtheritic paralysis.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **36**, 1246.

From a study of the cerebrospinal fluid in six cases of post-diphtheritic paralysis, Lavergne concludes that (1) localized palatal paralysis and polyneuritis are both accompanied by a meningeal reaction. (2) This is characterized by increased glucose and globulin content of the fluid, the cell content remaining normal ('dissociation albumino-cytologique'). (3) Probably this reaction appears earlier than the paralytic symptoms and an increase of glucose is the first manifestation. The reaction persists until recovery. F. M. R. W.

Dana, C. L. Wounds of the head and compensation laws. *Arch. Neurol. & Psychiat.*, 1920, **4**, 479.

According to Dana there are yearly two and a half million accidents to workmen in the United States, which cost the state 120 million dollars. In New York State alone there are two and a half million workmen subject to compensation laws (80 per cent. of total). In 1919 over a quarter of a million injuries were reported among these. 57,000 received compensation to the total amount of twelve million dollars, of which only 180,000 dollars went in medical treatment. In New York State a workman rendered unfit for two weeks receives medical attention and twenty dollars a week for two months; his disability is then assessed by a State Industrial Commission. At the end of this period many continue to complain of symptoms. About 15 per cent. of these suffer from nervous symptoms and many of them have received head injuries.

Those whose head injuries have not resulted in any destruction of the brain all show a very definite and constant syndrome. They complain of headache, vertigo, sleeplessness, irritability, asthenia, and defect of memory. The list of symptoms given by Chatelin and de Martel as the result of trivial head injuries in warfare is a replica of this.

Dana thinks it probable that in all cases of direct severe blows on the head there is some contusion of the brain, though of trifling degree. He classifies the patients as follows: In 10 per cent. of compensation cases these symptoms exist and suffice to make the patient uncomfortable. In a larger percentage—more than 50 per cent.—there is, in addition, anxiety, lack of concentration, and depression. The patient has never been ill before and cannot understand why the doctors do not cure him, and he asserts his desire to return to work. He becomes self-centred, exaggerates, refuses to attempt work or to do anything except to submit himself to fresh treatments. In a final class Dana includes patients, more numerous some races than in others, who from the beginning or after the suggestion and sympathy of their relatives and friends develop a definite attitude of exaggeration and tend to become frank malingerers. They consider their symptoms in terms of money and ultimately develop definite hysterical symptoms.

He considers that the psychology of such patients is simple and does not involve subconscious factors very much. Most of them are extremely dull and ignorant and do not appear to have any organized subconscious or directing complexes. They are uncomfortable, suffering, anxious, apprehensive, and live in hope of getting a sum of money. In other cases they are enjoying for the first time the luxury of an idle life with a weekly dole for which they do not have to work.

To label these patients psychoneurotics is an unworthy evasion. They are merely suffering from antisocial reactions to a painful injury. Most of them could be relieved or cured if taken in hand at once and carefully diagnosed and treated. The vast sums spent in compensation would be better expended in taking this problem in hand on such a basis. The compensation laws should be so modified that every patient receives early expert treatment, both surgical and neurological; that treatment and re-educational measures should be early and actively employed, and structural damage to the nervous system should be carefully excluded as a preliminary. F. M. R. W.

X. Jahresversammlung der Gesellschaft deutscher Nervenärzte in Leipzig, 1920. Pathologische Anatomie und Klinik der traumatischen Schädigungen des Rückenmarks. [**Pathological anatomy and symptomatology of injuries of the spinal cord.**] *Neurol. Centralbl.*, 1920, **39**, 631.

O. Marburg divided injuries of the spinal cord on a histological basis into (i) traumatic haematomyelia, (ii) traumatic softening, and (iii) traumatic meningopathy. The mechanism of these three forms of pathological lesion he explained as follows: Trauma causes at once a great rise of pressure within the blood-vessels leading to the partial or complete rupture and destruction of their walls. The lymph channels may be similarly affected. In the less severe injury we get haemorrhages; in the more severe, stasis, thrombosis, and softening. The lymphorrhages also facilitate softening. The meningeal lesions arise as follows: extradural haemorrhage leads to proliferation and thickening of the theca, while proliferation of the endothelium lining the dura leads to the formation of adhesions between dura and arachnoid. Coagulation of lymph and endothelial proliferation lead to adhesions between arachnoid and pia with loculation of the cerebrospinal fluid and fibrous thickening of the arachnoid (*Arachnoiditis serosa cystica et fibrosa*). The pia itself is relatively little involved. Primary lesions of the nerve elements have not been definitely established. When these structures are injured it is probably from vascular and spinal root lesions. The study of traumatic cord lesions affords no grounds for believing that chronic nervous diseases (syringomyelia or traumatic tabes) can arise in this way.

Dealing with the *symptomatology* of cord injuries, Cassirer makes a clinical division into cases with initial signs of a total cord transection with no recovery, cases with initial signs of total transection but with rapid improvement, and cases with the symptoms of various partial lesions. As to the relative frequency with which the different levels of the cord were involved, he had seen 70 cases with cervical lesion, 98 with thoracic lesions, 48 lumbar cord lesions, and 100 cases of injury of the cauda equina.

Total cord transections result in a flaccid paraplegia with loss of all reflexes, as Bastian described. But cases presenting this clinical picture immediately after injury may later recover, indicating that Bastian's law indicates only physiological interruption and not necessarily anatomical division. It is clear from Cassirer's review that, as far as the experience gleaned in Germany during the war goes, it approximates with that gained in France and in this country, but it is evident also that the investigation and analysis of total cord lesions in this country by Head and by Riddoch go far beyond anything attained in Germany, which appears to have nothing to teach us in this connexion. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Nakayama, Y. Observations on changes in virulence of haemolytic streptococci, with special reference to immune reactions. *J. Infect. Dis.*, 1920, **27**, 270.

The author records the influence of culture media and the reaction of the medium on virulence. Using haemolytic streptococci he gives tables showing that for the mouse a streptococcus from the heart-blood of another mouse has greater virulence than the same streptococcus grown on serum broth or agar.

Using blood agar with varying quantities of peptone, he shows that the peptone medium cultures have a higher virulence than blood agar without peptone. Cultures grown on acid medium are shown to have greater virulence than those grown on alkaline medium. Cultures grown anaerobically are shown to have greater virulence than those grown in the presence of oxygen.

Experiments are detailed which demonstrate the increase of virulence which occurs on passage through rabbits and mice, and also the increase in virulence of streptococci in a collodion sac implanted in the peritoneal cavity of a rabbit.

The agglutinability of streptococci was then tested after each of a series of passages with sera made from the original strain and from the last of a series of five passages. The table given shows that the more strictly homologous serum shows a higher agglutinating titre.

Similar relations appear to hold in the case of opsonins and precipitins.

The antigenic property of a streptococcus could not be shown to be altered by animal passage. G. T. W.

Meyer, Jacob. Opsonic reactivation of antipneumococcus serum. *J. Infect. Dis.*, 1920, **27**, 82.

The possibility of reactivating antipneumococcus serum as regards its opsonic power by the addition of small amounts of fresh normal serum was tested for a representative each of Types of I, II, III, and IV of pneumococci.

It was found that the addition of fresh normal serum markedly increased the opsonic activity of antipneumococcus sera of Types I and IV for the homologous cocci. No increase was noted on the addition of fresh normal serum in the case of Types II and III.

The sera of five cases of lobar pneumonia obtained subsequent to crisis was shown to possess considerable opsonic activity. This activity was largely destroyed by heating to 56° C., and was restored on the addition of fresh normal serum. One experiment in each series is detailed.

G. T. W.

Oliver, W. W. A rapid method of pneumococcus typing. *J. Infect. Dis.*, 1920, **27**, 310.

The method described consists in taking 1–1·5 c.c. of sputum containing pneumococci, adding to this 0·5–0·8 c.c. of normal saline gradually while stirring vigorously, and then adding 3–5 drops of ox bile and placing in a water-bath at 45–48° C. for 10–20 minutes. The solution is then filtered or centrifugalized and the filtrate or supernatant fluid used for carrying out precipitin tests with type sera. It is claimed that typing may be carried out in 30 minutes.

A table is given showing the results obtained in 25 cases where the method was controlled by Avery's method and by mouse inoculation.

In every case where a positive test was obtained for Types I, II, or III it was confirmed by Avery's method.

In 15 cases the test was negative. In 11 of these 15 Avery's method showed a Type IV, and in the remaining 4 cases there was a streptococcus.

G. T. W.

Wherry, W. B., and Butterfield, C. T. Inhalation experiments on influenza and pneumonia and on the importance of spray-borne bacteria in respiratory infections. *J. Infect. Dis.*, 1920, **27**, 315.

These experiments were carried out with sputum and the washings from tonsillar swabs from cases of clinical influenza. The sputum from 38 cases was used, examined, and *B. influenzae* isolated in 12 cases.

A variety of animals were sprayed with sputum obtained from these cases. Of 33 white mice so treated 4 died of primary pneumonia and 9 of a general infection with *B. enteritidis*, Type M 5. Of 5 guinea-pigs 2 died of a primary pneumonia and M 5 was isolated from the lungs.

The significance of these results is discussed, bearing in mind the fact that spontaneous infections with M 5 occur in these animals, and the suggestion is made that something in the influenza sputum causes some injury predisposing to such infection.

In support of the view that some predisposing factor must precede or accompany the implantation of bacteria in the lung the authors record that of 29 mice sprayed with a virulent culture of pneumococcus none became infected.

Further, they show that when animals are sprayed with cultures of M 5 and killed within 30 minutes, the bacilli can be isolated from the deepest portion of the lung in every case.

Similar results were obtained with pneumococci sprayed to mice. If, however, the animals are allowed to live they do not develop pneumonia, and on examining the lungs at a later date they yield sterile results.

G. T. W.

Moody, W. B., and Irons, E. E. On the occurrence of haemolytic streptococci in the stools of scarlet fever. *J. Infect. Dis.*, 1920, **27**, 363.

The stools of 85 patients with scarlet fever were examined by plating out on 10 per cent. goat blood agar. In all, 309 examinations were made, and haemolytic streptococci were isolated from 26 of the 85 patients.

The 26 strains were tested on media containing lactose, mannite, salicin, and inulin. They all fermented lactose and salicin and not mannite or inulin.

These streptococci bear no relationship to the duration of the disease, character of the stool, or age of the patient.

Eleven of these strains were tested for opsonic and agglutination reactions with the serum of a sheep immunized against streptococci obtained from the throat of an early case of scarlet fever, which results do not appear to have been satisfactory, and cannot have any significance.

G. T. W.

Holman, W. L. The bacteriology of epidemic influenza, with a discussion of *B. influenzae* as the cause of this and other infective processes. *Publ. from the Univ. of Pittsburg School of Med.*, 1919, 161.

This paper gives an account of the bacteriology of the influenza epidemic as observed in Pittsburg in the autumn of 1918. Subsidiary investigations were made into the presence of *B. influenzae* in the nasopharyx and agglutinins in the blood-serum, but chief attention was paid to the bacteriology of fatal cases, complete examinations being made in 32 autopsies carried out by Dr. Oskar Klotz and described in the same publication.

Films were stained by Gram's method and counter-stained by dilute carbol-fuchsin, while cultures were made on human blood agar, heated blood agar, and Loeffler's serum. The value of heated blood agar for the growth of *B. influenzae* is confirmed, rich cultures being obtained in some cases in which human blood agar gave negative results. Unaltered blood agar, however, gave a more useful picture of the general flora of a specimen.

B. influenzae was grown from 25 of the 32 autopsies. The author had reason to believe that it was probably present in all, but isolation was prevented by an over-growth of post-mortem contaminations.

It is the logical view to look upon *B. influenzae* as the cause of influenza, although proof is lacking.

The paper concludes with a detailed review of the bacteriology of *B. influenzae* and its relation to influenza. P. F.

Kellert, E. The pathological histology of tonsils containing haemolytic streptococci. *J. Med. Research*, 1920, **41**, 387.

The part played by the tonsils as the primary foci of generalized infections has been the subject of much investigation, and more writing, during the last two decades, although the question is not yet definitively settled. The present author has concentrated his attention on the pathological anatomy of 70 pairs of excised tonsils in which haemolytic streptococci had been demonstrated. All the specimens were obtained from adults—mostly soldiers. He found, as others have done, that enlarged and infected tonsils are of common occurrence in healthy adults, the largest tonsils not necessarily being the most severely infected. Large crypts favour the accumulation both of pathogenic and non-pathogenic bacteria, and in nearly all the specimens examined there were changes suggestive of an inflammatory reaction. There were, however, no changes distinctive of streptococcic infection. W. B.

Cannon, P. R., Dragstedt, L. R., and **Dragstedt, C. A. Intestinal obstruction: a study of the influence of the bacterial flora on the toxaemia of acute obstruction.** *J. Infect. Dis.*, 1920, **27**, 139.

The authors have carried out experiments to ascertain whether toxaemia, following artificially produced total obstruction of the gut in white rats, can be influenced by changes in the intestinal flora prior to the obstruction. They express the opinion that the toxic substances present in the obstructed intestine are produced by the action of bacteria on proteins or their split products.

Following on other workers, experiments were carried out which show that the bacterial flora of the intestine may be changed in character by diet. Three diets were used:

1. *Stock,* containing oats, cabbage, and carrots.
2. *Meat,* containing beef, cabbage, and carrots.
3. *Lactose,* containing whole milk, whole wheat bread, lactose, and cabbage.

The faeces of the animals were plated out and the relative number of 'aciduric' and 'proteolytic' types of organisms were estimated. This is termed the C-A ratio, Coliform bacilli being taken as representative of the proteolytic types. The C-A ratio in diets 1 and 3 is shown in the tables given to vary about 3–97, whereas on diet 2 it is reversed to about 95–5.

Rats on these diets were submitted to operation producing complete obstruction of the distal end of the caecum. After operation the same diets were continued. Death occurred in all cases in times varying up to 11 days. In all cases the picture at necropsy was to type, and the gut contained great preponderance of proteolytic bacteria.

Animals having great preponderance of 'aciduric' bacteria prior to operation did not retain this preponderance but showed a complete change to proteolytic flora in spite of the diets fed. The onset of toxaemia may, however, be delayed in the case of animals with an 'aciduric' flora. No detail is given of the method of arriving at the relative proportion of proteolytic bacteria. G. T. W.

Osborn, S. H., and Beckler, E. A. Once a typhoid carrier, always a typhoid carrier. *J. Infect. Dis.*, 1920, **27**, 145.

This paper contains a few notes on the typhoid carrier problem based on the records of 51 known carriers in the State of Massachusetts. A table is given of these 51 cases, recording occupation, year of infection, period before which any known cases of typhoid were caused, number of cases apparently due to carriers.

During 1918 and 1919, 132 cases, or 7·9 per cent., of 1,665 cases of typhoid in the State were caused by carriers. Of the 51 carriers studied, 21 transmitted the infection by milk and 18 others were food handlers. The opinion is expressed that 'once a typhoid carrier, always a typhoid carrier' holds good, but no new evidence is offered in support of this statement.

G. T. W.

Tenbroeck, C. A group of paratyphoid bacilli from animals closely resembling those found in man. *J. Exper. M.*, 1920, **32**, 19.

The author has made some investigations on two cultures of the bacillus isolated by Hirschfeld (1919) during an epidemic of clinical paratyphoid fever which occurred in Serbia, and which he named Paratyphoid C. Homologous serum for Hirschfeld's cultures was found to agglutinate to titre two strains of hog-cholera bacillus while *B. schottmülleri*, *B. enteritidis*, and swine typhoid bacilli were agglutinated in only the lowest dilutions. Biochemically, it was found, however, that Hirschfeld's bacilli fermented dulcitol and arabinose, produced hydrogen sulphide, and were non-pathogenic for rabbits. When fed to a pig a febrile condition resulted, from which the animal recovered. On the fifth day after the administration of the bacilli, hog-cholera virus was injected intramuscularly, with the result that the animal died in eight days with characteristic lesions of hog-cholera. From a number of sites bacilli were isolated which differed in certain respects from the cultures of the bacillus originally fed to the animal in that they more nearly resembled typical hog-cholera bacilli. W. B.

Tenbroeck, C. Bacilli of the hog-cholera group (*Bacillus cholerae suis*) in man. *J. Exper. M.*, 1920, **32**, 33.

The author has isolated a number of paratyphoid bacilli from a variety of animals, and on examining their cultural and biochemical properties has found they correspond to *B. paratyphosus* B. He points out that when bouillon cultures are used as antigens the animal paratyphoids can be separated by the type of clumping in the presence of an immune agglutinating serum. Absorption tests also separate the animal and human strains. Among the animal strains themselves no differential characters were noted, and the author suggests that at present they should be provisionally named from the animal in whose body they were found. Evidence exists that these micro-organisms have been associated with outbreaks of food poisoning in man, especially of the paratyphoid B type. The new group is distinct from such 'paratyphoid' bacilli as *B. cholerae suis, B. Voldagsen, B. abortus equi,* and *B. enteritidis,* all of which have also been found in animals. W. B.

Levine, Max. **Dysentery and allied bacilli.** *J. Infect. Dis.*, 1920, **27**, 31.

This paper records the results obtained from an investigation into the biological reactions of 111 strains of dysentery and allied bacilli. These 111 strains included:

B. dysenteriae, Shiga, 17.
B. ambiguus, 5.
B. dysenteriae, Flexner, 60.
B. alkalescens, 12.
B. dispar, 11.
Miscellaneous, 6.

These various strains were tested for acid production and indol. The test substances used were mannitol, lactose, glycerol, dextrin, dulcitol, sucrose, xylose, raffinose, and rhamnose. The results justify the conclusion that the main groups of bacilli can be differentiated by fermentation reactions. The author agrees that subdivision of the *B. dysenteriae,* Flexner, group into its serological groups is not possible by means of fermentation reactions.

Experiments were carried out to ascertain whether *B. alkalescens* and *B. dispar* can be differentiated from other strains by the rate of acid production and reversion to the alkaline. The medium used consisted of peptone 1 per cent., dipotassium phosphate 0·4 per cent., and glucose in amounts varying up to 0·5 per cent. A table is given showing that *B. alkalescens* and *B. dispar* form acid from glucose rapidly and revert rapidly (3–4 days), whereas *B. dysenteriae,* Shiga, and *B. dysenteriae,* Flexner, and *B. ambiguus* remain acid or revert slowly.

By increasing the peptone in this medium to 1·5 per cent. reversion to alkaline is said to be still more rapid in the case of *B. alkalescens* and *B. dispar.* The author agrees that many indicators show distinctly inhibitory action, especially for strains of *B. dysenteriae,* Shiga, and suggests a medium containing dipotassium phosphate, peptone, lactose, and glucose with roseolic acid and China-blue. G. T. W.

Meyer, K. F., and **Neilson, N. M.** **Irregular typhoid strains and the infections caused by them.** *J. Infect. Dis.*, 1920, **27**, 46.

This is a detailed study of three cases of infection with typhoid bacilli which show variations from the normal. The suggestion conveyed is that a person immunized artificially against typhoid may become infected, and that when this occurs the bacilli may be so altered in their characters as to be missed, and further, that such bacilli on gaining access to an unimmunized person regain their typical characteristics.

Case I was a caretaker in the laboratory animal room, who had charge of numerous animals which were infected with typhoid. This man was inoculated against typhoid and paratyphoid, three injections having been given two years prior to infection.

Case II was a laboratory worker who was handling specimens from Case I. This individual had also received the T.A.B. vaccine one year previously.

Case III was the father of Case II and was uninoculated.

From Case I an atypical strain of *B. typhosus* was isolated from the blood-stream on one occasion, his Widal reaction, stools, and urine always remaining negative.

Case II showed an irregular strain of *B. typhosus* in her urine on one occasion. This strain corresponded with that isolated from Case I.

Case III showed typical typhoid bacilli in the stools and urine.

This case appears to have been infected from Case II by handling an infected spatula twelve days prior to the onset of illness.

The chief irregularities shown by the strains isolated from Cases I and II were that they rapidly fermented dulcite, rhamnose, and gave irregular results with arabinose. They were agglutinable in living suspensions but were typhoid-inagglutinable in formalinized suspensions. Typhoid immune rabbits are protected against these strains. Antisera prepared from these irregular strains agglutinated typhoid bacilli in living suspensions only.

G. T. W.

Mayer, A., Guieysse, Plantefol, et **Fauré-Fremiet.** Lésions pulmonaires déterminées par les corps vésicants. [**Pulmonary lesions caused by blistering agents.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1532–5.

The inhalation of blistering agents such as dichlorethyl sulphide causes pulmonary lesions which differ greatly from those due to suffocating gases and which are characterized by immediate destruction of tissue, this being associated with the phenomena of congestion, oedema, and necrosis. Moreover, the lesions have a peculiar topographical distribution resulting from the fact that they act in the form of very minute drops. These have a destructive local effect, but do not cause any remarkable alteration in areas immediately adjacent, which may present an almost normal aspect.

The lesions are generally diffuse throughout the whole respiratory tract and have everywhere the same essential characters. The first phenomena of congestion, oedema and necrosis, are rapidly followed by the formation of tenacious diphtheroid pseudo-membranes, haemorrhages and numerous abscesses. These are, in the lungs, the direct cause of infarctions and of the production of large pneumonic foci alternating with simple atelectatic areas. The process generally ends in gangrene, but anatomical recovery is not impossible. This appears to be due to a proliferation of connective tissue vegetations, which are richly vascularized and provided here and there with cubical epithelium. Nevertheless, there is no real functional recovery, as the affected areas seem unable to take part any longer in the respiratory function. Death, when supervening, appears to be due to the obstruction of the gaseous exchange by the primary lesions as well as to a mechanism similar to that found in fatal and severe forms of broncho-pneumonia.

C. d. F.

Mayer, A., Guieysse, A., et Fauré-Fremiet, E. Lésions pulmonaires déterminées par les gaz suffocants. [**Pulmonary lesions due to suffocating gases.**] *Comp. rend. Acad. d. sc.*, 1920, **170**, 1289–91.

Fauré-Fremiet, E. Action de différents composés chimiques sur la cellule épithéliale pulmonaire. [**Action of various chemical substances on the pulmonary epithelium.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1344–7.

Guieysse-Pellissier, A. Modifications et lésions des cellules épithéliales pulmonaires dues aux gaz suffocants. [**Lesions of pulmonary epithelial cells due to suffocating gases.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1411–14.

Mayer, A., Magne, H., et Plantifol, L. Mécanisme de la mort dans le cas d'œdème pulmonaire aigu causé par l'inspiration de vapeurs ou de gaz nocifs. [**Mechanism of death in cases of acute pulmonary oedema due to inhalation of suffocating gases.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1421–4.

Investigations were first made on sections of lungs cut by means of a freezing microtome without any previous fixation. Different substances, either in a fluid or gaseous state, were made to act on such sections mounted in a drop of Ringer's solution to which a trace of dahlia violet had been added. The effect of the various substances was systematically watched under the microscope. By this method it has been possible to establish that the normal equilibrium of pulmonary epithelial cells becomes differently modified by the action of such substances as alcohols, ethers, mineral and organic acids, &c. These modifications, when slight, appear as phenomena of precipitation and dissolution of one or the other of the constituents, the epithelial cells, viz. phosphatides appearing as mitochondria, lipoid rich in cholesterol, gel-containing albuminoid materials, and forming the fundamental substance of the cell bodies.

These changes are 'reversible', viz. the cells may recover if the action of the above-mentioned chemicals is stopped in time. But if prolonged or allowed to be excessively felt, death of the affected cells may result either from a form of general coagulation of the cytoplasm or through a process of more or less complete cytolysis.

These observations are of interest because they help one to understand the cytological changes observed when employing very small doses of irritant and other gases such as were lately used in warfare. For instance, the lesions caused by suffocating gases in the epithelium of the trachea and bronchial tubes do not essentially differ from those described above, particularly if the gases have acted for a very short time. If the action has been more powerful the simple phenomena of agglutination of the cytoplasm and of dissolution of the intracellular inclusions such as the mitochondria, are rapidly followed by necrosis of the epithelium which becomes detached from the congested and oedematous submucosa. Similar phenomena can be observed in the lungs, though the picture is here much altered by the acute oedema and the rapidly following small-celled infiltration, which form the chief lesions caused in the lungs by suffocating gases. Moreover, the reaction of the pulmonary tissues to small doses of irritant or suffocating gases is characterized by a rapid multiplication of the less affected epithelial cells. This may be very intense and generally leads, through amitotic and incomplete divisions, to the formation of multinucleated cells similar to megakaryocytes. These are often seen lying free in the alveoli, where they apparently assume the rôle of scavenger cells, afterwards undergoing processes of degeneration and fragmentation until they ultimately disappear.

These various changes end generally in a more or less complete recovery, both anatomical and physiological, though areas of splenization, viz. of a tissue functionally inactive, may also form.

If the quantity of inhaled poisonous vapours has been rather large, death generally follows even before histological changes have had time to make their appearance. The authors accept the theory that death results in such cases from impaired oxygen supply, this being due to the acute oedema itself and to the consequent formation in the lung alveoli of a thick fluid layer separating the air from the blood.

These various results, though interesting, do not differ essentially from those obtained in this country since 1918 by the Chemical Warfare Medical Committee appointed by the Director-General, A.M.S. (The Reports of this Committee were issued by the Medical Research Committee during the war as confidential documents. Copies have since been presented to the principal medical libraries in Great Britain.) C. d. F.

Fauré-Fremiet, Guieysse, Magne, et **Mayer, A.** Lésions cutanées déterminées par certains composés vésicants. [**Cutaneous lesions caused by certain blistering agents.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1476–9.

The investigations were carried out with dichlorethyl sulphide. This, when applied to the skin, produces a remarkable congestion associated with a certain degree of oedema as in the case of certain corrosive caustics. As a result of prolonged application blisters are formed which remind one of those due to drugs used for therapeutic purposes, such as cantharides; however, in the case of dichlorethyl sulphide, the lesions of the cells of the Malpighian layer seem more severe as no cell-divisions can be traced in the affected areas. C. d. F.

Mayer, A., Magne, H., et **Plantefol, L.** (1). Réflexes provoqués par l'irritation des premières voies respiratoires. [**Reflexes produced by irritation of the upper respiratory passages.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1206.

Mayer, A., Magne, H., et **Plantefol, L.** (2). Action réflexe produite par l'irritation des voies respiratoires profondes. [**Reflex action due to irritation of the deep respiratory passages.**] *Compt. rend. Acad. d. sc.*, 1920, **170**, 1347–9.

If irritant gases are made to act on the nasal mucous membrane, respiration becomes at first both shallow and slow and then quickly stops. At the same time there is a slackening of the rate of the heart and manifestations of a general vasoconstriction. But if the upper respiratory passages are painted with cocain, or if the trigeminus is cut before the experiment with irritant gases begins, no respiratory stoppage takes place. Hence the conclusion that this is of reflex origin and due to the excitation of the nerve-endings of the fifth cranial nerve. If the animals experimented upon are very sensitive, e.g. rabbits, or if the gas used is particularly irritant, the intensity of the resultant reflex is such that breathing suddenly stops and cannot be re-initiated by artificial respiration, even if this is prolonged for 15–20 minutes. Oxygen is without any effect, as, indeed, during all the time of the experiment the quantities of O consumed and of CO_2 produced steadily diminish. This is taken to show that the irritation of the fifth cranial nerve is sufficient not only to stop breathing but also to cause a 'reflex' reduction of the gaseous exchange of the animal.

If the same irritant gases are made to act only on the bronchial tubes and deep respiratory passages, changes of a different kind can be observed. In fact breathing becomes very rapid and quickly transformed into a true polypnoea. This, according to the author, is also a reflex phenomenon due to excitation of the pneumogastrics. Indeed it no longer appears if, before the inhalation of the irritant vapour, these nerves are cut, and it ceases suddenly if they are cut during the experiment.

If the irritant gases are allowed to act simultaneously on the whole of the respiratory system, two antagonistic actions are caused at the same time and the respiration shows a simultaneous and equally irresistible tendency to stop and to accelerate. In such a case breathing becomes greatly spasmodic and convulsive and death from suffocation rapidly ensues.

C. d. F.

Levaditi, C., et **Harvier, P.** Recherches sur le virus de l'encéphalite épidémique. [**Researches on the virus of epidemic encephalitis.**] *Compt. rend. Soc. de biol.*, 1920, **83**, 1140.

The previous researches of the authors have already been abstracted (vide *Medical Science* 1920, **2**, 285, 572). They showed that the virus of encephalitis is communicable through the anterior chamber in rabbits. In the present paper they find that after intra-ocular injection of virus the retina and the optic nerve are infective and cause intense encephalitis and meningitis. They also show that the disease can be transmitted by the mucous membrane of the nose, which has been artificially inflamed by means of croton oil. Filtrates made from the mucous membrane of rabbits dead from encephalitis did not reproduce the disease. Virulent cerebral material injected into the testicle of the rabbit determined encephalitis after an incubation period of 7 days and the virus was found to persist in the testicle for at least 17 days. In their previous papers the authors showed that a primary inoculation of encephalitic virus did not produce immunity against the virus of poliomyelitis. In the present communication they show the converse also obtains. Poliomyelitis virus does not protect against encephalitis virus. There is, in fact, no cross-immunity indicating that the diseases are not identical.

W. B.

Fildes, P., Parnell, R. J. G., and **Maitland, H. B. Unsuspected involvement of the central nervous system in syphilis.** *Medical Research Council. Special Report Series*, No. 45, 1920.

This paper refers to a continuation of previous work (vide *Medical Science*, 1920, **1**, 624).

Fildes, Parnell, and Maitland did not find such a high percentage of cases showing pathological changes in the cerebrospinal fluid as has been recorded by other observers. They attribute this result to the large number of cases examined, and also to the exclusion of doubtful cases. Taking 10 cells per cubic millimetre as the index of a pathological condition, and 5 to 9 cells as representing doubtful cases, they obtained a percentage of 18 which showed undoubted pathological changes in the cerebrospinal fluid, in a series of

1,314 men the great majority of whom were in the early stages of syphilis and showed no obvious signs of nervous disease. If doubtful cases are included the percentage was 28. In those cases in which the disease was of more than 18 months' duration (also without symptoms of nervous disease) the percentage rose to 34.

It is noteworthy that in four cases these changes in the cerebrospinal fluid were present before the Wassermann reaction in the blood had become positive, thus demonstrating that the central nervous system may be involved at a very early date after infection. The nature of this pathological condition they regard as a syphilitic meningitis—an opinion which they base not only on the presence of lymphocytes in the cerebrospinal fluid, but also on the frequent occurrence of polymorphonuclear leucocytes in the more pronounced cases. In a large proportion of the cases the Wassermann reaction in the fluid was positive, and in one case *S. pallida* was found by dark-ground illumination.

These cases were characterized by the almost total absence of symptoms, and few showed any clinical signs even after careful examination of the motor and sensory functions, and the eyes. In early primary syphilis there were no clinical signs, but, in the later stages, symptoms such as headache, giddiness, facial and ocular paresis or paralysis were noted in some cases, and also slight but definite changes in the fundus oculi, which were regarded as representing early stages in the development of choroido-retinitis.

With regard to the effect of treatment on these conditions, in some the cerebrospinal fluid was rapidly changed to normal, and in others there was marked improvement. On the other hand, some cases were resistant to treatment, and the meningitis progressed in spite of repeatedly renewed treatment, which consisted in intravenous injections of neosalvarsan or its equivalents, but no mercury.

As regards the bearing of these early pathological changes in cerebrospinal syphilis on the future development of cerebral syphilis or 'parasyphilis', the authors point out that a series of prolonged observations are necessary before this can be decided. They point out, however, that the proportion of cases showing early pathological changes is apparently large, while the proportion of those who develop general paralysis is small. They suggest that those cases which subsequently develop general paralysis have persistently positive Wassermann reactions in the cerebrospinal fluid. In view of the importance of early treatment, and also for diagnostic and prognostic purposes, they advise lumbar puncture as a routine measure in the examination of all cases of syphilis. C. F. M.

Lundie, C., and **Goss, F. H. Observations on the sporulation of the syphilis organism.** *Lancet*, 1919, ii, 1025.

In scrapings from syphilitic chancres, examined by dark-ground illumination, Lundie and Goss observed the discharge of numerous refractile granules from leucocytes. They believe that these granules represent sporulation of the spirochaetes. They also found flagellate organisms which discharged diplococcal bodies, and short spirochaetes possessing only a few spirals. They suggest that these phenomena represent different stages in the life-cycle of the *Leucocytozoon syphilidis* described by McDonagh.

C. F. M.

Manouélian, M. Y. Tréponéma pâle et anévrisme aortique. [***Treponema pallidum* and aortic aneurysm.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, 3e sér., **44**, 742–7.

Manouélian describes two cases of aortic aneurysm in which he found *Treponema pallidum.* The organisms were few in number and scattered in the peripheral layers of the aneurysm. They were demonstrated in sections treated by the silver nitrate method. C. F. M.

Pinard, M., et Hoch. Présence de tréponèmes dans le sperme. [**The presence of treponemes in the semen.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, 3e sér., **44**, 762–3.

The experimental inoculation of apes and rabbits, by Finger and Landsteiner, with human semen from cases of secondary syphilis showed that the latter is capable of conveying contagion; but most observers have failed to find the treponema in the semen. Pinard and Hoch, however, report that they have demonstrated its presence in three out of eleven cases. In the first case the infection was of one year's duration and secondary syphilides of the buccal cavity and genitals were present. The second case was one of early secondary syphilis with roseola. No testicular lesion was evident in these cases. None of the patients had received arsenical or mercurial treatment. The preparations were made by washing the semen several times with normal saline, centrifugalization, and staining with the Fontana-Tribondeau method. Pinard states that he also saw the treponema in one case by the dark-ground method as long ago as 1910. C. F. M.

Foulerton, A. G. R. On poisoning by arsenobenzol compounds used in the treatment of syphilis. *Brit. M. J.*, 1920, i, 864–7.

The question of poisoning by arsenobenzol compounds has been investigated by Foulerton by means of experiments on animals. His primary object was to determine whether the benzene constituent of these compounds aggravated the toxic effects of the arsenic. For this purpose rabbits were injected subcutaneously with: (1) arsenic oxide; (2) the benzene constituent (ortho-amido-phenol); (3) arsenobillon and kharsivan). The results of these experiments are as follows:

(1) the injection of arsenic oxide produced interstitial hepatitis with fatty infiltration of the liver, and in severe cases changes of the parenchymatous cells. Nephritis was also present. In two cases fatty infiltration of the liver and kidneys produced an appearance which was exactly comparable to that seen in poisoning by arsenobenzol. (2) Injection of ortho-amido-phenol also caused acute hepatitis and nephritis and fatty infiltration of the interstitial tissue, also parenchymatous changes. (3) Injection of the two arsenobenzol drugs gave the same histological appearances as those found in the less acute cases of poisoning by arsenic oxide. These experiments show that the fat-metabolizing functions of the liver are directly affected by the action of arsenic oxide in poisonous doses. But, in view of the serious damage to the liver and kidney caused in experimental poisoning by ortho-amido-phenol, it is probable that the toxic action of the arsenobenzol compounds is influenced to some extent by the benzene constituent. Foulerton points out that evidence of poisoning by arsenobenzol being due to the action of arsenic alone is furnished by the fact that toxic jaundice with fatty infiltration of the liver

and kidney may be caused by poisoning with arseniuretted hydrogen gas. It is also shown by the case treated with Fowler's solution mentioned above.

Discussing the practical bearing of these cases of arsenical poisoning on the treatment of syphilis, Foulerton thinks that the risk of poisoning by arsenobenzol is difficult to estimate, since these special toxic effects were not generally recognized during the whole of the period when these drugs were in common use, and the deaths recorded probably only represent a fraction of those attributable to this cause. The effects being essentially due to arsenic, probably intensified by the benzene constituent, further observations are required to show the proportion of the two ingredients which produces the least toxic effect.

Foulerton also remarks that the possible effects of mercury on a liver already more or less damaged by the toxic action of arsenical compounds require further consideration. In a case of poisoning with mercuric chloride, he found hepatitis and fatty infiltration of the liver and also intense nephritis, and is, therefore, of opinion that even moderate doses of mercury may have an injurious effect on a liver already damaged by arsenic in the modern 'intensive' treatment of syphilis. For this reason he considers it advisable that simultaneous treatment by arsenic and mercury should be discontinued. He also recommends that patients should be kept under careful medical regimen throughout the period of treatment and for some weeks afterwards, and that the diet should be regulated so as to lighten the work of the liver as much as possible, by the avoidance of milk and fatty foods.

C. F. M.

Silbergleit, H., u. Föckler. Ueber das Auftreten von Ikterus und akuter gelber Leberatrophie bei Syphilitikern im Anschluss an Neosalvarsanbehandlung. [**On the occurrence of jaundice and acute yellow atrophy of the liver in syphilitics, following the administration of neosalvarsan.**] *Ztschr. f. klin. Med.*, 1919, **88**, 333.

During the last few years there has been a remarkable increase in the number of cases recorded of acute yellow atrophy of the liver, a condition formerly regarded as a great rarity. A preponderating factor in this increase has been alleged to be salvarsan in one or other of its different modifications, as the cases have occurred in syphilitics who have been treated with arsenical preparations. Some investigators have, however, denied the influence of salvarsan, and believe that the condition is essentially due to syphilis itself or in combination with some other unknown factor. Strange to say, the majority of the cases have borne the salvarsan treatment apparently without ill effect, but perhaps some weeks later have been seized with jaundice, drowsiness, acute delirium, and have died in a few days, the autopsy showing changes, especially in the liver, of an acute destructive character. The present authors have reported in detail a remarkable outbreak in which 13 fatal cases occurred, between the end of December 1917 and the beginning of March 1918, in the Reservelazarett in Ingolstadt, a military hospital for the treatment of venereal and skin diseases. In addition to the 13 fatal cases there were 8 others who were severely ill with jaundice but escaped with their lives. In the period in question 110 other syphilitics were treated without accident, and none of the 215 skin or gonorrhoeal cases were attacked. The salvarsan and the technique of administration were apparently perfect. The cases were in various stages of syphilis, from early to late, and one indeed had congenital syphilis with a negative W.R. Where examined, no spirochaetes were found in any of the fatal cases. The authors make an exhaustive analysis of the causes of the fatality, including a discussion of the possibility of a Weil or other spirochaetal infection, and ultimately admit that they were unable to solve the mystery. Of particular importance is the record of a further fatal case in which no history of syphilis or antisyphilitic treatment could be elucidated. It was that of an assistant surgeon, aged 24½ years, who served at the front during 1914–17, when he was captured by the French. Being released, apparently in perfect health, in November 1917, he was detailed to the syphilitic department of the Ingolstadt hospital, treated some of the fatal cases up to December 1917, and actually made a *post mortem* on one of the cases of acute yellow atrophy on December 27. He cut his finger at the autopsy, but there was no local inflammation. On February 6, 1918, he was transferred to the hospital in Erlangen, was taken ill there on March 7 with all the characteristic symptoms of acute yellow atrophy, from which he succumbed on March 10. Subsequent inquiries failed to elicit any history of syphilis or antisyphilitic treatment. He was not engaged on any work in connexion with poisons, and there was no evidence or suspicion of suicide from poisoning or other cause. Although there was no evidence of lues the authors think it *may* have been present, and possibly he may have received ambulant salvarsan treatment. His W.R. was negative. W. B.

De Witt, L. M., Suyenaga, B., and Wells, H. Gideon. The influence of creosote, guaiacol, and related substances on the tubercle bacillus and on experimental tuberculosis. *J. Infect. Dis.*, 1920, **27**, 115.

This paper concerns a number of experiments which have been made to determine whether there are any experimental grounds for the use of creosote, guaiacol, and related substances in the treatment of tuberculosis. Virulent tubercle bacilli were exposed to the action of the drug, and it was found that growth was inhibited on artificial media containing 0·01 per cent. (1 : 10,000) of resorcin, thymol, paracresol, orthocresol, or metacresol. With guaiacol, creosote, hydroquinone, and guaiacol cacodylate the concentration had to be increased to 0·1 per cent. (1 : 1,000) completely to inhibit growth. The bactericidal effect of these substances was also found to be slight. When tubercle bacilli on garnets were exposed to solutions of the drugs, and were subsequently injected into guinea-pigs, it required an exposure of 20 minutes to a 0·5 per cent. concentration of creosote or guaiacol to kill most of the bacilli. In other series of experiments guinea-pigs were rendered tuberculous and were subsequently treated by the drugs in question, administered intracardiac, intramuscularly, or subcutaneously. The drug, far from curing, seemed to have lowered the resistance of the animals, as the controls did not show such extensive infection *post mortem.* While, therefore, there appears to be no well-founded basis for the belief that creosote and similar compounds act on the tubercle bacillus they may have some action on the secondary agents of infection in pulmonary tuberculosis.

W. B.

Novick, N. The incidence of bovine infection in tuberculous meningitis. *J. Med. Research*, 1920, **41**, 239.

The author has examined 48 strains of tubercle bacilli isolated from guinea-pigs which had been injected with cerebrospinal fluid from 48 unselected cases of tuberculous meningitis, mostly in children. Four of the cases were aged 15, 16, 24, and 32 years respectively. The usual methods of diagnosis were employed, including the virulence test in rabbits. Of the 48 strains only 3 answered to the bovine type, one being a child 6 years old which had been breast fed, the second a child 22 months old, while the third was 16 years of age and had a tuberculous family history. The research was carried out in the laboratory of the New York Board of Health.

W. B.

Hektoen, L. Further observations on the effects of roentgenization and splenectomy on antibody production. *J. Infect. Dis.*, 1920, **27**, 23.

The author has in previous papers shown that roentgenization of white rats, dogs, and rabbits, at the same time as antigen is introduced, may greatly diminish antibody production; further, that splenectomy just prior to injection of antigen causes a lower antibody curve.

In the present paper experiments are recorded showing that in white rats the amount of lysin produced for sheep's corpuscles may be diminished by splenectomy at the time that the blood was injected. These results, however, do not appear to be uniform when using other animals and different corpuscles as antigen.

If splenectomy is not carried out until antibody production has got well started it does not appear to have any marked effect. Further, if splenectomy is combined with roentgenization at or near the high point of the curve of immunization there is no marked effect in the curve of antibody production. Roentgenization 16 days before injection of antigen may increase antibody production; the results of such experiments, however, appear to be uncertain.

G. T. W.

BIOCHEMISTRY

Henderson, Y., and Haggard, H. W. The elimination of carbon monoxide from the blood after a dangerous degree of asphyxiation, and a therapy for accelerating the elimination. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 11.

Poisoning by carbon monoxide produces permanent effects when lack of oxygen has caused death of cells. It is, therefore, important to restore the oxygen-carrying power of the blood as soon as possible. Breathing oxygen is beneficial in two ways: it supplies more oxygen in solution in the blood and displaces carbon monoxide from the haemoglobin. During the onset of carbon monoxide poisoning overbreathing occurs so that carbon dioxide is washed out of the circulation. Later, respiratory ventilation is diminished until sufficient carbon dioxide has accumulated to stimulate the respiratory centre.

Curves of elimination of carbon monoxide are given showing that administration of oxygen increases elimination of carbon monoxide. Carbon dioxide also assists elimination by increasing respiratory movements. A combination of oxygen with carbon dioxide is more efficient than either separately. These results indicate that in places where there is a danger of carbon monoxide poisoning a supply of oxygen and carbon dioxide should be available, so that a mixture of 90 per cent. oxygen and 10 per cent. carbon dioxide may be administered as soon as possible.

H. E. R.

Allan, W. The effect of emetin on *Entamoeba histolytica* in stools. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 21.

Emetin does not kill *Entamoeba histolytica* in strengths less than 1 : 2,000 in one or two hours. Solutions of 1 : 150 often failed to kill them in the allotted time. H. E. R.

Norgaard, A. Über die Pepsinbestimmung in achylischen Probemahlzeiten mit besonderer Berücksichtigung der Adsorption von deren festen Teilen. **[On pepsin estimation in 'achylic' test meals, with especial reference to the adsorption of solid parts.]** *Biochem. Ztschr.*, 1920, **107**, 145.

An error in pepsin determinations in test meals, when no free HCl is present, may arise from the fact that in the absence of free HCl pepsin will not pass through the filter-paper. It is adsorbed in some way upon the solid particles of the meal. This may be shown by taking an achylic test meal, dividing into two portions, filtering one portion immediately, and letting the other stand with added HCl before filtration. The former will show no pepsin values, the latter will. For clinical purposes the author recommends working with Mett's technique upon unfiltered test meals.

R. A. P.

Rosenthal und **Holzer.** Beiträge zur Chemie des Blutes bei anämischen Krankheitszuständen. **[On the chemistry of the blood in anaemic conditions.]** *Biochem. Ztschr.*, 1920, **108**, 220.

The experiments deal with the theory of Tallquist and Faust of the origin of anaemias, in which they attributed them to the presence in the blood of substances of an oleic acid nature. This has been brought up in modified form by Eppinger, King, and Medak. The authors here cannot find any difference between the cholesterin, cholesterinester, and iodine value of the fats in the bloods from cases of anaemia and those from healthy cases. After splenectomy in man, there was no real fall in the unsaturated fatty acids in the blood, nor did the iodine value run parallel to the intensity of blood destruction. The spleen itself does not contain increased quantities of unsaturated fatty acid in bad cases of anaemia. The red corpuscles in pernicious anaemia are free from cholesterinester. The oleic acid theory of anaemias is therefore not confirmed.

R. A. P.

Verzár u. **Bögel.** Untersuchungen über die Wirkung von akzessorischen Nahrungssubstanzen. **[Experiments on the effect of accessory food factors.]** *Biochem. Ztschr.*, 1920, **108**, 185.

In order to get information as to how the accessory food factors produce their effects, the authors have tried the physiological effects of extracts of fat-soluble *A*, and water-soluble *B* vitamines, using as pure extracts as possible. The main result was that *B* extract produced vasoconstriction and *A* extract vasodilatation. Both extracts produced a depression of the heart-beat, when perfused through frogs' hearts—this however could be restored by subsequent return to the ordinary Ringer perfusion. Experiments of this nature are being continued.

R. A. P.

Stepp, W. Über das Vorkommen von aldehydartigen Substanzen im Blute von Kranken. [**On the presence of aldehyde substances in the blood of diseased persons.**] *Biochem. Ztschr.*, 1920, **107**, 60.

The paper deals with carbohydrate metabolism, from the standpoint of health, diabetes, and kidney disease. A good number of diabetics and nephritics have substances in the blood showing the properties of aldehydes. For instance, these substances react with iodine in alkaline solution to form iodoform, they reduce Fehling's solution, and ammoniacal silver nitrate, and are destroyed by heating with silver oxide. They are apparently not acids with aldehyde properties, and the probability seems strong that the substance is acetaldehyde. In certain diabetic cases these substances were absent, and there was no fixed ratio between the amount of sugar in the blood and of these aldehyde substances. The author does not consider that the hyperglycaemia in diabetes can possibly be explained in terms of an increased sugar mobilization, but thinks that there are deep-seated changes in the processes of sugar katabolism. R. A. P.

Andree, W., und **Wendt, H.** Über den Einfluss einiger darmwirkender Arzneimittel auf die endogene Harnsäureausscheidung. [**On the influence of some intestinal medicines upon the endogenous uric acid excretion.**] *Biochem. Ztschr.*, 1920, **107**, 50.

The authors have found that aperients (such as senna, Epsom salts) and substances such as bismuth subnitrate do not change the endogenous uric acid excretion. Any variations which occurred in their experiments lay within the normal limits for the individuals experimented upon.

R. A. P.

Starkenstein, E. Die Beeinflussung des Purinhaushalts durch Atophan, Calciumsalze und Radium-Emanation. [**The influence upon purin metabolism of atophan, calcium salts, and radium emanation.**] *Biochem. Ztschr.*, 1920, **106**, 139.

The injection of doses of atophan (phenyl cinchoninic acid) is followed by a great increase of the uric acid excretion. The day after taking the atophan, the uric acid excretion falls below the normal. Calcium salts in doses of 16 grm. per day cause a decrease of uric acid excretion. Radium emanation causes an increase of uric acid excretion in man and animals. Experiments upon the allantoin excretion in animals, and perfusion experiments upon the liver are also reported. The author thinks that the effect of atophan is to mobilize uric acid from the stores present in the body. This he considers to be due to a lowering of the kidney threshold of excretion, though he thinks also that there is a 'hindering' effect upon the whole purin metabolism produced by atophan. R. A. P.

Brinkmann u. **Dam.** Studien zur Biochemie der Phosphatide und Sterine. [**Studies on the biochemistry of phosphatides and sterins.**] *Biochem. Ztschr.*, 1920, **108**, 35.

These three papers deal with the question of haemolysis, and an antagonism of action between lecithin and cholesterin. If rabbits' corpuscles are put directly into hypotonic salt solution, haemolysis will take place, whereas if they are first washed twice with isotonic NaCl solution, and then put into hypotonic solution, no haemolysis will take place. A treatment of the washed corpuscles with serum again will, however, restore the original effect. This increase of resistance to haemolysis by the washing treatment is found to be due to the washing out of lecithin from the corpuscles, and does not occur if the corpuscles are washed in isotonic cane sugar solution. The power of lecithin in lowering the resistance of the corpuscles is apparently antagonized by cholesterin. These results, if further substantiated, are very suggestive in connexion with experiments upon the complements of the serum. The ratio lecithin/cholesterin is of direct importance, too (according to the authors), in questions of the electric isolation of the cell, the ionic permeability of the cell surface, and the water-content of the tissues. Lecithin feeding in rabbits was found to produce in a week an intensive intravital haemolysis. R. A. P.

Stoklasa, J. (with **Sebor, J., Zdobnicky, Napravil, E.,** and **Hromádko, J.**). I. Ueber die Radioaktivität des Kaliums und ihre Bedeutung in der chlorophyllosen und chlorophyllhaltigen Zelle. II. Der Mechanismus der physiologischen Wirkung der Radiumemanation und der Radioaktivität des Kaliums auf die biochemischen Vorgänge bei dem Wachstumsprozess der Pflanzen. III. Die Bedeutung der Radioaktivität des Kaliums bei der Photosynthese. [**I. On the radioactivity of potassium and its importance in the chlorophyll-free and chlorophyll-containing cell. II. The mechanism of the physiological effect of radium emanation and the radio-activity of potassium upon the biochemical change in the growth processes of plants. III. The importance of the radioactivity of potassium in photosynthesis.**] *Biochem. Ztschr.*, 1920, **108**, 109.

Some recent work in rather different fields is tending to show that we have to deal with the factor of radio-activity in ordinary physiological processes. In connexion with the heart, Zwaardemaker has claimed that the potassium in a perfusing Ringer's solution may be replaced with other radio-active elements such as thorium or uranium in the right proportions. Potassium has the distinction of being mildly radio-active. Zwaardemaker claims that physiological activity can be maintained intact after the substitution of uranium for potassium. It is perhaps worth mentioning that the experiments have been criticized by A. J. Clark, who holds that although uranium will excite a heart brought to rest by leaving out potassium from the perfusion fluid, it will not, nevertheless, maintain a normal heart-beat, showing that the function of potassium is one peculiar to itself.

Stoklasa's papers are of interest in connexion with this subject. He has shown that plants treated with radio-active water grow better than those which have not been so treated. Further, radio-activity influences the growth of germinating seeds; the seeds grow quicker when submitted to a mild intensity of radiation. This is even true for the action of the radiations from potassium. The synthetic processes are apparently quickened because it is found that radiation increases the formation of sugar and the building of NH_2 compounds. Further work established the fact that some plants were helped in their development by radium emanations whereas others were hindered. The key to the meaning of this was given by estimations of the potassium content of the plants. Those helped by the radium emanation were poor in their content of potassium, and those hindered the reverse. This rather leads to the conclusion that radiation is stimulating to the same sort of process as potassium.

The effect of light is interesting. Seeds radiated in the dark grow better than the controls in the dark; in the light the reverse happens. This shows that in some way the effect is to be correlated with photosynthesis. An additional piece of evidence upon the supplementary effect of potassium and radiation is got from some experiments upon killing bacteria. Bacteria rich in potassium are killed more easily by radium emanation than bacteria poor in potassium.

The correlation of radio-activity, potassium, and the effect of light led to the experiments described in the third paper. Stoklasa does not consider that magnesium is concerned with the photosynthetic processes of the plant directly. He finds that the absolute essentials for growth of plants are phosphorus and potassium. Experiments show that mixtures of CO_2, $Mg(OH)_2$, and H_2 do not give any formation of formic acid, formaldehyde, or sugar when treated with the ultra-violet rays. On the other hand, mixtures of KOH, CO_2, Fe, and H_2 have given noticeable amounts of hexose when treated with radium emanations, and lower derivatives have been observed for similar mixtures with the action of the ultra-violet rays, and radiation even when K has not been added.

The upshot of all this is that Stoklasa infers that in the mechanism of photosynthesis the sun's radiant energy is connected with the energy of the β-rays and γ-rays sent out by the potassium. R. A. P.

Mertz, A. Bemerkungen zur Mikrobestimmung des Traubenzuckers nach dem Verfahren von J. Bang. [**Remarks on Bang's latest method for the estimation of sugar in blood.**] *Ztschr. f. physiol. Chem.*, 1920, **111**, 43.

Mertz produces experiments to prove that the method of indirect heating suggested by Bang in his last communication on the determination of blood-sugar was a real advance in technique. When pure chemicals are employed the alkaline iodate mixture is quite stable. C. G. L. W.

Stoltzenberg, H., und **Stoltzenberg-Bergius, M.** Über Melanin und Humus. [**Melanin and Humus.**] *Ztschr. f. physiol. Chem.*, 1920, **111**, 1.

An organic chemical paper in which certain relations are pointed out which exist between benzo-quinone and the black pigments found in various occupational cancers, ochronosus, &c. C. G. L. W.

Plaut, R. Über den Einfluss des Ovarialhormons auf das Beckenwachstum. [**Ovarial hormones and pelvic development.**] *Ztschr. f. physiol. Chem.*, 1920, **111**, 36.

The ovaries of cows were extracted with ether, and the extract freed from phosphatides with acetone. An olive oil solution of the hormone was made which was injected subcutaneously into rabbits, guinea-pigs, and cats.

The results were most marked in rabbits. The upper symphyseal angle which is acute in 5–12 weeks old rabbits (58–75°) becomes obtuse in older rabbits (110–120°). In rabbits treated with the hormone the angle was increased (75–90°). The pelvis becomes transversely wider and longitudinally shorter, thus approximating the adult pelvis.

The extract exercised its effect on all three classes of animals. The action is specific, for the lipoid extract of placenta and of the ovarial tissue freed from corpora lutea is inactive. The uterus and vagina of a guinea-pig treated with the extract in large doses were hypertrophic.

C. G. L. W.

v. Euler, H., and **Svanberg, O.** Über Giftwirkung bei Enzymreaktionen. IV. Electrometrische Messungen über die Bindung des Silbers und des Kupfers an Saccharose und an andere organische Verbindungen. [**Toxic action of silver and copper on enzymes.**] *Fermentforsch.*, 1920, **4**, 142.

The authors have determined by means of silver and copper concentration chains that a certain amount of the metals enters into combination with the enzyme. The preparation used was a very highly purified saccharase. The toxic action on the ferment is in relation to the amount of metal combined. Copper is relatively non-toxic. Experiments with certain organic substances appear to show that the toxicity of the metal is connected with a SH-group in the saccharase molecule. One molecule of toxic substance combines with one molecule of ferment, and this combination is inactive. A full discussion of the problem is given.

C. G. L. W.

Hoskins, H. D., and **Osgood, E. E.** **Modification of van Slyke's titration method for estimating the alkali reserve of blood.** *J. Lab. & Clin. M.*, 1920, **6**, 37.

The method of van Slyke is modified by using larger flasks (120 c.c.) for mixing and matching colour; another use of turbid colour standards made by adding a small amount of maize starch. The difficulty of matching is thus removed. C. G. L. W.

Jackson, D. E., and **Raap, G.** **An experimental investigation of certain features of the pharmacological action of salvarsan.** *J. Lab. & Clin. M.*, 1920, **6**, 1.

First-class preparations of salvarsan have almost no direct action on the musculature of the dog. Acute symptoms resembling anaphylactic shock or the so-called 'nitritoid crises', if produced by good preparations of salvarsan, cannot be due to a spasmodic contraction of the bronchioles.

C. G. L. W.

RADIOLOGY AND ELECTROLOGY

Radiography.

Parola, L., e **Celadar, A.** Quadro radiologico delle vere cisti ossee solitarie. [**Radiological picture of true single bony cysts.**] *Radiol. med.*, 1920, **7**, 83.

The author gives an historical survey of the pathological views, from Virchow's idea of softening of a chondroma to Mikulicz, who defined the benign osseous cyst as characterized by the substitution for natural bone of fibrous tissue rich in giant cells and susceptible of cystic softening. Mikulicz dealt especially with the group of benign solitary cysts, which he separated from other cavities in bone. They are like, but not identical with, the distrophic fusiform callus occurring sometimes after fractures. The author describes the typical history of local trauma, with no further pain or functional symptom until a spontaneous or easy fracture discovers the presence of a cyst. The local examination shows a single rounded or fusiform smooth swelling or expansion of bone, the consistency being hard, or yielding, with 'egg-shell crackling' sensation. The surrounding parts are not involved in any way. At operation is found a cavity containing some clear or blood-stained serous fluid. There is no periosteal change. The cavity is sometimes trabeculated. Operation leads as a rule to permanent cure.

Discussing the theories of the pathogenesis, the author quotes the view of Röpke and others, who believed in chronic or attenuated infection, and the theory of the traumatic origin of the cysts. He believes rather in an osteo-distrophy, the morbid process being due to fibrous osteitis upsetting the proper calcification and nutrition of the bone. Yet this does not fully meet the question, which is much too uncertain for dogmatism.

Some forms have neoplastic characters, and must be considered as cystically degenerated neoplasms. Others are not degenerations from morbid states, but are primitive forms, and benign. These are the benign solitary cysts and pseudo-cysts. The true cyst has its own surrounding membrane, the pseudo-cyst has no membrane.

The points in the differential diagnosis are:

(1) Radiology shows a progressively worse local condition while the general state is good.

(2) Local changes felt and seen.

(3) Functional impairment insignificant.

(4) Patients are all young.

(5) Treatment is always successful and patients go back to work.

The radiological points are:

(1) Regular and smooth cortex.

(2) Cavities are oval, fusiform, or triangular, with the base formed of the epiphysis and the truncated apex containing fluid.

(3) Transparency of cavity.

(4) Alterations of form, volume, and structure of bone. Uniform swelling externally, softening internally. Periosteum and soft parts not affected. True cyst shows clear margin. Fibrous cyst shows shading from centre to periphery.

(5) Trabeculae may give an areolar aspect. In the cyst of fracture callus there is a layered or striated effect.

The first four points are Beck's, who found the syndrome absent in a series of sarcomata. The author agrees substantially with Beck in this.

N. H. M. B.

JEWETT, C. H. Teleroentgenography of the sella turcica with observations on one hundred normal cases. *Am. J. Roentgenol.*, 1920, **7**, 352.

The author reports the results of an attempt to establish a definite standard of size and shape for the normal adult sella turcica, and an indication of the variations of the normal.

Teleradiography combined with stereoradiography is the best method of investigation. The sellae examined fall into eight groups according to their general structural characteristics. A brief description of each group is given and the findings summarized in a table. No definite relation is elicited between weight, height, age, or dimensions of cranium, and the size and shape of the sella turcica, except that the group (9 per cent. of cases) showing the highest average age is associated with very indistinct clinoid processes. Apparent absence of the processes does not *per se* appear to be of any pathological significance.

The author considers that unusual conditions of the sella turcica should be closely correlated with the clinical data before any conclusion is drawn from the radiological appearances.

E. M. W.

Radiobiology.

SEGALE, G. C. Sull' azione dei raggi Röntgen e del radium sulle cartilagini epifisarie. [**The action of X-rays and of radium on epiphysial cartilage.**] *Radiol. med.*, 1920, **7**, 234.

In considering the possible effects of radiation on this active and susceptible tissue the author puts five questions:

(1) What modifications in the growth of bone can be found to follow various conditions of treatment?

(2) Can development be arrested or checked?

(3) Are the lesions produced of temporary nature, susceptible of recovery, or are they permanent and progressive?

(4) What, if any, latent period is there?

(5) What histological change can be observed, and how does it affect the various elements?

His experiments were performed on 41 white rats, of several litters, all from 8 to 14 days old. Applications of X-rays or of radium were used.

The conclusions are:

(1) Even a small dose of rays applied to a growing limb inhibits growth. This is more marked with γ- and β-rays of radium than with γ-rays alone.

(2) The change begins quickly, the latent period for a medium dose is less than four days.

(3) The changes are not temporary and do not tend to recover, but rather to increase in severity, causing early arrest of growth.

(4) As shortening of the limb takes place there may appear curvatures

and deformities of bone. There is decreased thickness of the diaphysis and atrophy of muscles.

(5) One sees a degenerative process in cells and structural alterations in from 5 to 8 days after a fairly strong dose. These are fairly characteristic. There is no vascular change.

Later on, from 59 to 83 days, when development has been partly arrested by the rays, a characteristic structural change is evident, with diminished functional activity. β- and γ-rays from 20 mg. of Ra sulphate in one hour's application led two months later to a condition wherein the epiphysial cartilage had thickened but had lost its structural characteristics. There was almost complete absence of vascularity and the bony lamellae showed change. Radiation had arrested the function of ossification of cartilage.

(6) There is extra radio-sensibility of epiphysial cartilage in its active stage, and there is probably an alteration in the activity of osteoblasts.

N. H. M. B.

Radio-diagnosis.

Holmes, G. W. The radiographic findings in pericarditis with effusion. *Am. J. Roentgenol.*, 1920, **7**, 7.

From experimental laboratory work, this observer finds the radiographic demonstration of the heart within the pericardial sac in pericardial effusion is very difficult. Also, that when the pericardial sac is artificially distended with fluid, the cardiac outline becomes more rounded but the cardio-hepatic angle is not obliterated.

From clinical observations, the presence or absence of pulsation seems to depend somewhat on the amount of fluid present. Loss of pulsation, however, is found in cases of cardiac dilatation as often as in pericardial effusion. The cardio-hepatic angle was sometimes acute, sometimes obtuse, and sometimes obliterated, but this is equally true with dilatation. The angle is more likely to be obliterated if the patient is examined in upright position.

The author summarizes the findings in pericarditis with effusion as follows: An abnormally shaped heart shadow which changes with change of position of patient. Change in shape of the angle formed by the posterior border of the heart, the diaphragm, and the spine. Faint or absent pulsation.

R. W. A. S.

Loyer, C. Les os surnuméraires du pied. [**The supernumerary bones of the foot.**] *Thèse de Par.*, 1920. (*J. de radiol. et d'électrol.*, 1920, **4**, 471.)

The supernumerary bones of the foot, 8 in number, may be divided into two categories:

A. Those whose radiological image has not yet been obtained: (1) Supernumerary calcaneum (of which an example has been found in a mummy of Thebes), a small bone situated at the antero-internal angle of the large process of the calcaneum, protruding more or less into the scaphoido-cuboidal interspace, and usually more or less joined to one of these two bones. (2) Os uncinatum (Lilienfeld believed he saw it once on a radiograph), very rare, situated on the plantar surface of the 3rd cuneiform.

(3) Duplication of the 1st cuneiform into two distinct parts, one superior and dorsal, the other inferior and plantar. (4) Intermetatarsal bone (Lilienfeld claims to have seen it once by X-rays) situated in the posterior part of the 1st interosseous space, between the 1st cuneiform and the 1st and 2nd metatarsals.

B. Those found by radiography: As these are often cartilaginous they seem to be far less common to radiologists than to anatomists; and when seen on the plate may be mistaken for a fracture. (5) Tibiale externum was, in the early days of radiology, confused with a fracture of the scaphoid (Haglund's fracture); it may assume different appearances, according to its development; typically it is a hemisphere or irregular pyramid whose base corresponds with the tuberosity of the scaphoid on its postero-external side; it may be completely united to the scaphoid, may be free, or partly joined to it, thus rendering easy the confusion with a fracture. It may be a cause of trouble owing to the projection which it causes at the side of the foot; and it may be the seat, during the period of growth, of a painful inflammatory condition. (6) Os trigone, situated at the posterior part of the astragalus, sometimes free, sometimes joined to the latter (most of so-called Shepherd's fractures are in reality examples of os trigone). (7) Os peronale, a narrow elongated bone situated along and below the external edge of the cuboid. (8) Os vesaliane, situated at the posterior part of the 5th metatarsal, which it prolongs; it may be confused with an abnormal posterior epiphysial process, but may probably (Laquerrière and Drevon) co-exist with this anomaly. This bone is very rare. There only existed four radiological images of it up to the publication of the two cases in this journal, but the author found two more cases in Laquerrière's collection.

S. U. L.-B.

Mougeot, A., et **Pacaud.** L'aortite thoracique descendante: son diagnostic radioscopique. [**Radioscopic diagnosis of descending thoracic aortitis.**] *Paris méd.*, 1919, **9**, Nov. 8. (*J. de radiol. et d'électrol.*, 1920, **4**, 420.)

In all cases in which previous clinical examination had revealed or had led to the suspicion of an aortic lesion the authors systematically sought to examine the vessel both in its descending thoracic portion and in the ascending or transverse portions of the arch. Whereas the ascending aorta gives definite stethoscopic signs and the abdominal aorta presents symptoms obtained entirely by palpation combined with the graphic method, the descending thoracic aorta is inaccessible to clinical means of examination and can only be satisfactorily diagnosed by means of radiology. From this point of view, whenever anterior examination reveals an abnormal left aortic semicircle, the whole thoracic portion of the aorta should be examined in the oblique anterior right, the oblique posterior left, and the left lateral positions.

The aortic semicircle corresponds, not with the descending aorta, but with the arch and with its termination at the level of the left side of the 4th dorsal vertebra. With three orthodiagrams the authors show that the left edge of the shadow of the descending aorta, invisible when physiological, is clearly distinguished when pathological, that it departs markedly from the sternal line and terminates on the cardiac shadow, more or less on the outside, according to the degree of dilatation of the vessel, falling either entirely within the pulmonary curve or a little inside of the infero-external extremity of the pulmonary curve.

The initial portion of the descending aorta must be examined in the left lateral, or very obliquely in the left anterior oblique position.

The authors controlled the results of their observations by radiographic negatives taken on the cadaver after injecting into the right common carotid, under slight pressure, a mixture composed of water, plaster of Paris, and subnitrate of bismuth: their plates showed that the topography of the descending aorta does not correspond with the description given in recent treatises on cardio-aortic radiology, and they confirm the contradiction, already noted by Cerné, between the schemes of radiological examination of the descending aorta and the well-established findings of descriptive anatomy.

They affirm that the clear space is not situated between the descending aorta and the vertebral column, as is implied by present-day opinion, but between the two branches (ascending and descending) of the aorta. In a normal subject the descending aorta is invisible, being situated in the clear posterior space, of which the posterior limit is traced by the vertebral shadow, and the anterior by the ascending aorta above and the heart below. This space, invisible in a slightly oblique anterior right position, increases with the degree of obliquity. The shadow joined to the posterior part of the ascending aorta is mistaken, up to this point, for the descending aorta, but is in reality absolutely distinct from it, as is shown by very oblique examination. S. U. L.-B.

Radiotherapy.

Haxthausen. Roentgenulcerationer opstaaet 9 maaneder efter Bestraalingen. [**Development of Roentgen ulceration 9 months after treatment.**] *Hosp.-Tid.*, 1920, **63**, 40–1.

Haxthausen records the case of a woman, aged 52, who, a year and nine months earlier, was given X-ray treatment for severe metrorrhagia. A series of five exposures was given, the dose at the first exposure being 15 H. with a 3 mm. aluminium filter. At the next two exposures the same filter was used, but the dosage was increased to 25 H. At the two last exposures, the tube by a mistake was held too near the skin, and the dosage was, therefore, increased by an unknown quantity. Some weeks later an erythema appeared on the parts exposed (both nates); later, a weeping dermatitis developed, disappearing in a few weeks under treatment with ointments. Not till 9 months after the exposures did a second erythema appear in the same region. Infiltration of the tissues followed and was succeeded by ulceration. In spite of treatment with compresses, ointments, and light, there was no improvement 9 months later, when a large, dirty ulcer, measuring 8 by 8 cm., with sharply defined irregular margins, occupied the left nates. There was diffuse infiltration of the surrounding tissues with a broad, cyanosed, and hyperaemic zone about the ulcer. A similar but less extensive condition was found on the right nates. Commenting on this case, Reyn (*ibid.*) did not think that this ulceration could have been due to the omission of the filter by mistake, for had this been the case the ulceration would have begun much sooner. He was convinced that somehow or other an over-dosage had been given, and that the prognosis was bad because the ulceration had occurred in spite of the rays being filtered. C. L.

Serena, M. Di talune azioni a distanza prodotte dei raggi X. [**Certain actions at a distance produced by X-rays.**] *Radiol. med.*, 1920, **7**, 203.

A study of the effects of small or medium doses of X-rays which produced distant changes when applied to certain glands, apparently through the medium of an action on the internal secretions. Cases are quoted to show how a series of small stimulative doses applied to the thyroid or genital glands led to correction of menstrual functions and the clearing up of psoriasis and other dermatoses. The author regrets that there is no clue as yet to the proper dose of rays to the thyroid for procuring restoration of normal menstruation. N. H. M. B.

Gavazzeni, S. Due casi di tumore dell' ipofisi con sindrome acromegalica curati coi raggi X. [**Two cases of pituitary tumour with acromegalic syndrome cured by X-rays.**] *Radiol. med.*, 1920, **7**, 222.

One case had the complete clinical picture of acromegaly, and radiographically showed evidence of pituitary tumour. The symptoms of disease were of four years' standing, but the condition improved very much under X-ray treatment. The other case showed the same symptoms and signs in a milder degree, and the results of radiotherapy were equally good.
N. H. M. B.

Jaugeas. Contribution nouvelle de la radiothérapie des tumeurs hypophysaires. [**New contribution to the radiotherapy of pituitary tumours.**] *J. de radiol. et d'électrol.*, 1919, **3**, 508. (*Arch. d'électric. méd.*, 1920, **28**, 190.)

No affection enables one to judge of the deep action of X-rays, to control their efficacy, and to appreciate the value of technique better than the above-mentioned, thanks to the measurable variations in the patient's field of vision.

The author quotes observations on a woman of 25 presenting the classic symptoms of pituitary tumour with acromegaly. Radiography of the skull showed almost entire destruction of the sella turcica, a breaking-up of the floor of the cavity with opening of the sphenoidal sinuses. Disorder of vision first attracted her attention; an oculist advised recourse to radiotherapy. Twenty séances produced a very marked improvement in the condition of the sight. Examination of the visual region showed a temporal hemianopsia on the left side and a hemianopsic scotoma on the right.

Radiotherapy was continued for two years, employing two temporal and two frontal portals of entry for the rays, each of which received 50 H. every fortnight of a penetrating irradiation, filtered at first by 2 mm., then by 4 mm. aluminium. Improvement began from the first months of treatment. The scotoma disappeared; the two visual regions extended; visual acuity improved and became nearly normal. At the same time the general condition of the patient improved and she soon regained her intellectual activity. The improvement obtained might be considered as nothing more than an immediate and temporary effect of the radiotherapy, were it not that an older observation, in which the beneficent effect lasted for six years, permits one in this case to speak of a cure.

Treatment should always be begun early, when the syndrome of glandular hyperactivity is manifesting itself. It should be conducted with care, so as to preserve a sufficient functional value of the gland and to avoid production of a syndrome of insufficiency in place of that of hyperactivity, such as occurs in exophthalmic goitre. The visual field should serve as guide during progress of treatment. S. U. L.-B.

Radium Therapy.

Laseaux, R. Contribution à l'étude de la radiumthérapie associée à la chirurgie dans le cancer opérable de l'utérus. (*Thèse de Paris* 1919–20). [**Radium therapy and surgery in operable cancer of the uterus.**] *Presse méd.*, 1920, May. (*J. de radiol. et d'électrol.*, 1920, **4**, 427.)

It is possible that the future treatment of cancer of the neck of the uterus will be by radium alone, but for the present, surgical treatment having already been proved radium therapy must be linked up with surgery.

Radium therapy may be associated with three kinds of surgical intervention: vaginal hysterectomy, total abdominal hysterectomy, and extended abdominal hysterectomy (Wertheim's operation). If the first two are indicated in those special cases in which induration of the parametrium renders a very extensive intervention dangerous, Wertheim's hysterectomy remains the operation of choice in all cases in which the neoplasm is clearly localized.

The patient may be irradiated before operation, immediately afterwards, or a few weeks after cicatrization. Pre-operative irradiation is very advantageous; by diminishing the vitality of the growth, and by rendering the cervical cavity aseptic, it considerably lessens the risks of cellular and microbial inoculation; in some cases, too, by giving the uterus a certain mobility, it enables the limits of operability to be enlarged. But from this last point of view the contrary effect may be produced; by leading to the production of sclerosed tissue round the cervix and the vaginal dome, irradiation may render hysterectomy extremely dangerous. Immediate post-operative irradiation should be discarded, because of the dangers it entails. It risks adding to the shock of operation, induces an abundant exudation which increases the chances of infection in a cavity relatively ill-drained by the vagina, and also the proximity of the intestine creates a serious danger of eschars. This is not the case with delayed post-operative irradiation. This should be repeated whether the case be one of recurrence or not. From this variety of treatment a remarkable number of survivals after hysterectomy has been registered; in 1914 Henkel reported 17 successes in 17 cases; more recently Kelly reported 20 cures out of 20 cases; Iribane gives 4 cures out of 6. These few figures show that, save for coincidence, the association of post-operative radium therapy with hysterectomy gives better results than Wertheim's method alone, since this intervention, even in the hands of the ablest surgeons, only gives from 55 per cent. to 60 per cent. of clinical cures, and Demarest finds these figures above the average.

Irradiation should be repeated several times after operation at intervals of from one to three months. The doses employed will vary according to the result desired, but on this point authors do not yet agree.

S. U. L.-B.

Heyerdahl, S. A. Empirical results of the treatment of cancerous tumours with radium. *Acta Chirurgica Scandinavica,* 1920, **52**, 511.

Heyerdahl contributes a long article upon the treatment of malignant tumours with radium; the cases dealt with were in the main superficial, and the paper consists for the most part of clinical notes upon individual cases. We learn that the Röntgen-Radium Institute of the Riks Hospital, Christiania, has, for the general purposes of its radium therapy, 200 mg. of radium, which is used either in small platinum tubes or flat applicators.

In dealing with these superficial growths, extensive use is made of Kerr's paste. It is stated that this was first used by Dr. Edling, whose method of using it is as follows: The paste, when heated to 40°–50° C., becomes soft and pliable, and may take the form of the tumour to which it is applied; it becomes quite firm again at the temperature of the body. By the aid of the paste the radium tube or applicator may be securely fixed to tumours in different positions, as, for example, on the inside of the mouth. Reference to Dr. Edling's book, *Studien über Applicationmethoden in der Radiumtherapie,* gives us on p. 80 some additional information about this paste, which is known as Kerr's Perfection Impression Compound of the Detroit Manufacturing Co., Mich., U.S.A.

From the numerous illustrations in Heyerdahl's paper there is no doubt that in many cases the use of the compound solves very quickly the technical difficulties which arise in many radium applications. The paper will repay study from the purely clinical side.

S. R.

Pesci, E. Reazione de Wassermann nel cancro e sue modificazioni dopo la radiumterapia. [**The Wassermann reaction in cancer and its modifications after radium treatment.**] *Radiol. med.,* 1920, **7**, 196.

30 per cent. of cases of carcinoma show a positive Wassermann reaction with guinea-pig's heart for antigen. The cancerous serum loses its power of deviating the complement after repeated doses of radium treatment. The opposite has never been seen, a negative reaction has not been converted to a positive one as a result of irradiation, because the combination required is neutralized by the excess of albumin in the blood which follows radiation.

N. H. M. B.

Electrotherapy.

Dowse, C. M., and **Iredell, C. E. The effective resistance of the human body to high-frequency currents.** *Arch. Radiol. & Electroth.,* 1920, **25**, 33.

The expression for the heating effect, C^2R, which obtains for a continuous current C flowing through a conductor, resistance R, is changed completely when high-frequency currents are employed, the latter consisting usually of repeated trains of undamped waves, whilst the resistance of the conductor may be very different from its value for direct current. However, if C be the reading of a hot wire ammeter and R be the resistance for high frequency, the simple expression may be used.

By applying Lord Rayleigh's formula giving the relation between the continuous and high-frequency current resistances for a straight round conductor to the case of a limb, the 'skin effect' for a frequency of $10^6 \sim$ per second is found to be very small. The 'skin effect' in metallic conductors is considerable for this frequency, and to reduce the energy loss all parts of a diathermy apparatus should be connected by short conductors consisting of many well-insulated strands.

When two electrodes are held firmly and a high-frequency current is passed through the body, small leaky capacities are considered to exist at both ends of the body-resistance between the electrodes and the mass of tissues, which are separated by the skin and a small air-space. In parallel with this circuit is one due to the small capacity between the body and the earth. The impedance of such a circuit was determined, the resistance term of which is the only one responsible for heat production. The effective impedance for a simple resistance in parallel with a capacity is $\frac{Re}{\sqrt{1+p^2 C_e^2 R_e^2}}$, where $p = 2\pi x$ frequency, which at frequency $= 10^6 \sim$ per sec., approximates to $\frac{1}{pC_e}$.

The resistance of the human body to high frequency was found by a substitution method, the testing current being reduced as low as possible to avoid variations in temperature.

High-frequency oscillations were obtained from a glass plate condenser in series with a spark gap and a coil of two turns of stranded wire, the primary of an oscillation transformer of variable coupling. The gap was connected through choking coils to the secondary side of an iron core transformer giving 750 volts. The secondary coil of the oscillation transformer was connected through a high insulation switch, allowing either the body or a variable resistance to be included in the circuit, to a short length of high-resistance wire in metallic contact with a copper-constantan thermojunction, a sensitive moving coil galvanometer forming the indicator. The most suitable variable resistance was a burette full of copper sulphate solution, the variation being obtained either by dilution or by altering the distance between the copper electrodes immersed in it, and was standardized against a definite length of Eureka wire.

By varying the pressure at the point of contact of one electrode and the arm, the other electrode being firmly bound, it was found that the resistance for high frequency from the upper part of the flexor surface of the forearm to the anterior surface of the upper arm decreased by 30 per cent. as the pressure increased to 50 gms. per sq. cm. Whether the hands holding short tubular electrodes be dry or well wetted by a solution of common salt the impedance was found to be 575 ohms. Evidently the resistance effect of the skin is very small.

The equivalent resistance between the hands was tested before and after passing a small direct current for five minutes with the bare palms in a saline solution. A reduction amounting to less than 2 per cent. was found.

The resistance between the hands for a number of individuals was found to vary from 450 to 650 ohms.

When a diathermy current was passed from hand to hand, the equivalent resistance with both arms flexed was 440 ohms, whilst when they were extended it was 526 ohms. The resistance of the hand and a finger was

390 ohms with the finger straight, 380 ohms when bent perpendicular to the palm, and 310 ohms when flexed until the distal part was almost parallel to the palm. It was found that the apparent resistance of the trunk between the deltoids was only 45 ohms.

Measurements of the equivalent resistance were made on two subjects before and after the passage of a high-frequency current of 5 ampères at a high voltage for five minutes, the rise in temperature being 2° F. In both cases the resistances decreased by 12 per cent. Warming the hands beforehand produced no effect on the equivalent resistance.

On testing the equivalent resistance at different frequencies it was found that the results differed considerably from the theoretical values. Using a bridge and balanced telephone method a series of low-frequency tests were made to ascertain the value of any capacity effects, and to investigate the nature of any changes in resistance and capacity with frequency. Although no appreciable capacity effect was found in the liquid resistance, it was found that on replacing it by the hands holding cylindrical electrodes no balancing resistance could be found to give silence in the telephone, but a well-defined minimum was obtained. A variable condenser across the balancing arm could be adjusted so that the sound in the telephone was almost inaudible. As the frequency was increased from 50 ~ per sec. the actual resistance and capacity diminished, but the latter more quickly than the former. The effective resistance $\frac{R}{1+p^2C^2R^2}$ is nearly R at low frequencies, since C is very small. If it be assumed that the resistance of the body at a frequency of 10^6 ~ per sec. is the same as at 1,000 periods, in the author's case 1,050 ohms, the capacity calculated from the impedance is ·00025 *mfd.* From analogy with dry insulators, the authors conclude that the effective resistance of the body at high frequency is much lower than for low-frequency current. Assuming that the actual resistance of the body is reduced to 800 ohms at 10^6 frequency, the value of the effective resistance would be 430 ohms, less than half that for low frequency.

L. H. C.

REVIEW

EPIDEMIC HICCOUGH AS A MANIFESTATION OF LETHARGIC ENCEPHALITIS[1]

Although persistent hiccough was recorded as a striking symptom in connexion with the recent epidemic of influenza in this country, it has not been generally identified since as a possible symptom of lethargic encephalitis. Yet in France last winter, and to an even greater extent during the present winter, it is attracting a considerable amount of attention. It appears to be widespread, and there is general agreement in regarding it as the expression of a mild form of encephalitis. There is some reason to suppose that it is also occurring in England, and that those in general practice are seeing at the moment cases of persistent hiccough in unusual frequency. Probably the trivial nature of the symptom and its disappearance in a few days is responsible for the absence of published accounts of the condition in this country. Clearly, if the view of the French observers is correct, as it seems to be, it is of some importance that observers in this country should have their attention drawn to this manifestation of a disease that in its more severe forms might constitute a grave problem of public health.

In January 1920, Sicard and Kudelski, in one of their descriptions of the so-called 'myoclonic' encephalitis, recorded the appearance of clonic spasms of the diaphragm with or without hiccough. Simultaneously Dufour recorded 11 cases in which hiccough was the sole somatic nervous symptom. Of these, 10 ran a benign course and consisted of an attack of four days' duration, showing slight fever, malaise and persistent hiccough followed by recovery. One case went on to generalized 'myoclonus', mental disorders and death. The cases of Sicard and this last case of Dufour went a long way to establish the identity of 'epidemic hiccough' and encephalitis.

During the present winter a large number of cases of 'epidemic hiccough' have already been recorded in France by Sicard and others.

The general character of the illness appears to be as follows. There may be a short prodromal period of several days during which the patient complains of lassitude, generalized pains, headache and epigastric discomfort. There may be slight fever during this period. Hiccough then appears and persists in short attacks of from 15 to 30 minutes about every half hour for three or four days. On the other hand, it may come on suddenly in an individual in apparently perfect health; as Sicard says, 'C'est soudainement au milieu de la vie sociale ou professionnelle que la secousse diaphragmatique se produit et que le hoquet éclate'.

While it lasts there is slight fever. Usually the pulse-rate is normal, though some cases are recorded in which there was tachycardia. The cerebrospinal fluid is normal, and there are no other objective manifestations of the disease of any kind. The attack passes off as suddenly as it began, but while it lasts no artifice seems of value in stopping the hiccough. Rivet, however, mentions that it may be controlled by pressure upon the globes of the eyes. Relapses are not seen, and the vast majority of cases are males. In Paris in two instances, two bank clerks occupying the same desk were almost simultaneously affected.

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[1] This review was received for press too late for inclusion in its proper place.

Netter and Vincent, discussing the possibility that suggestion may be in part responsible for the widespread incidence of this syndrome, conclude that the inclusion of the sternomastoids and scalene muscles in the spasm, the grunting character of the sound (in distinction to the loud bark of the hysteric hiccough), and the frequent unilateral character of the diaphragmatic contraction exclude hysteria as in any important measure concerned. While, in addition, Sicard's cases of clonic spasm of the diaphragm without hiccough also point to this conclusion.

In short, then, epidemic hiccough appears as a brief illness of from one to five days' duration ending in recovery. It is characterized by attacks of hiccough (about 6 to 10 to the minute) frequently repeated over this period and accompanied by slight fever and malaise. A short prodromal period of fever, pains, and malaise may precede the actual hiccough.

Achard, Ch., et **Rouillard, J.** Hoquet épidémique. *Bull. et mém. Soc. méd. d. hôp. de Paris,* 1920, 3e sér., **36**, 1534.

Dufour, H. Le hoquet épidémique. *Bull. et. mém. Soc. méd. d. hôp. de Paris,* 1920, 3e sér., **36**, 263.

Rivet, L. A propos du hoquet épidémique. *Bull. et mém. Soc. méd. d. hôp. de Paris,* 1920, 3e sér., **36**, 1541.

Sicard, J. A., et **Kudelski.** Encéphalite myoclonique à secousses prédominantes abdomino-diaphragmatiques. *Bull. et mém. Soc. méd. d. hôp. de Paris,* 1920, 3e sér., **36**, 121.

Sicard, J. A., et **Paraf, J.** Le hoquet épidémique. *Bull. et mém. Soc. méd d. hôp. de Paris,* 1920, 3e sér., **36**, 1484.

F. M. R. W.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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REVIEWS

TUBERCULOSIS

Epidemiology. Kieffer's analysis of his 2,312 cases at the Municipal Hospital for diseases of the lungs, Mannheim, shows that the ratio of females to males has markedly increased owing to the war, the rise being from 42 per cent. in 1912 to 56·4 per cent. in 1919. He correlates this increase with the wholesale employment of women on war work. Thus, before the war only about one-third of the adult female population was engaged in industrial occupations, whereas in 1916–19 more than three-quarters were thus engaged. With regard to a family history, one or both parents were tuberculous in 732 cases, or about a third of the total. The younger the patients, the more frequent were the family histories of tuberculosis, and among the 194 patients under the age of 10, there was a history of tuberculosis in the parents in 130, i. e. in more than two-thirds of the total. The proportion of cases with a family history showed a marked decline during the war. Thus, in 1912–14, 58 per cent. of 788 patients gave a family history, whereas in 1918–19 only 36·5 per cent. of 655 patients gave such a history. The younger the patient the more frequently were sources of infection found; among patients under 6 the sources of infection could be traced in almost 90 per cent.

During the war many cases of pulmonary tuberculosis were observed among well-developed, athletic persons, and hardly 20 per cent. exhibited the *habitus phthisicus*. But this *habitus* was often associated with a comparatively benign form of the disease, whereas it usually ran a rapidly fatal course in well-developed patients. In this connexion Kieffer suggests that a previous tuberculous illness is associated with a comparatively mild form of the disease later in life, the immunity conferred by a prolonged, clinically demonstrable form of early tuberculosis being greater than that following a slight primary infection without clinical manifestations. During the war the percentage of cases terminating fatally within a year rose steadily from 25 to 59. The war also changed the morbid anatomy of the disease, the fibroid type largely giving place to the ulcerating, rapidly progressive type. In the period 1912–14, the ratio of 'closed' to 'open' forms of pulmonary tuberculosis was as 1 to 0.9. By 1919 this ratio was as 1 to 2·3. If only children under 10 were considered, this comparative increase of the number of 'open' cases was still more marked, the respective ratios being 1 to 1·16 and 1 to 5·6.

Langendörfer, of the Medical Polyclinic in Bonn, has investigated the fate of the 269 children of 50 families during the war in each of which one or other of the parents suffered from tuberculosis. As many as 77 or 28·6 per cent. of these children were already dead, the cause of death being tuberculosis in 60 or 22·3 per cent. Of the surviving 192 children of various ages up to 20 years, 86 or 44·7 per cent. were suffering from tuberculosis. Thus, 146 or 54·2 per cent. of the total of 269 children had contracted their parent's disease. By various regroupings of his figures, Langendörfer shows that the mortality among the children was greater when the mother suffered from tuberculosis than when the father was diseased. Both the morbidity and mortality from tuberculosis among the children were higher in large than in small families, and the later-born suffered more often from tuberculosis than the first-born. As for the age incidence, both the morbidity and mortality were greatest in the first 5 years of life, and in the period just before and after puberty.

Tuberculosis in the first-born. Hansen, who in 1915 confirmed Karl Pearson's conclusions as to the comparative susceptibility of the first-born to fatal pulmonary tuberculosis, draws attention to the significance of Kjerrulf's investigations. These show that, early in life, the first-born are not more often infected with the tubercle bacillus than the later-born. It cannot, therefore, be argued that the greater mortality of the first-born from tuberculosis is due to earlier infection; the 'soil' and not the 'seed' must be held responsible for the high death-rate from tuberculosis among the first-born.

Mortality. The recent enormous increase in the mortality from pulmonary tuberculosis in Buda Pesth is illustrated by Engel as follows: In 1914, 13·9 per cent. of the deaths were due to this cause; in 1915, 15·7 per cent.; in 1916, 23·4 per cent.; in 1917, 23·3 per cent.; and in the first half of 1918, 25·2 per cent. The mortality from tuberculosis in Hungary was 15·4 per cent. in 1916, 15·8 per cent. in 1917, and 18·3 per cent. in the first half of 1918. The increase in the mortality was only in part due to fresh infections, a considerable proportion of the mortality being due to the effect of privations and hardships or cases which had occurred before the war.

Parisot, of Nancy, who was consultant to the French army of occupation for six months, states that in Germany, and especially in the Rhine provinces, the mortality from tuberculosis was progressively diminishing before the war, and in 1914 did not exceed, and in many cases did not reach the figure of 20 per 10,000 in towns and 15 per 10,000 in the country districts. In 1914 the number of deaths from tuberculosis was approximately half of what it was in 1900. On the other hand, the influence of the war on the tuberculosis mortality was shown by a progressive increase in the death-rate, which was more marked and rapid in the urban than in the rural population, so that in large towns such as Mayence and Frankfort in 1918–19 the mortality from tuberculosis was approximately double what it was in 1914. As regards the proportion of deaths at various ages, the mortality from tuberculosis diminished in the case of children during the first year of life—a fact explained by the fall in the birth-rate—remained stationary from 1 to 5 years, and showed a slight increase from 5 to 15 years. The mortality was more than doubled for persons aged from 15 to 30 (327 deaths in 1918 as compared with 144 in 1914 for a population of 400,000 inhabitants), amounted to 534 as compared with 323 deaths between 30 and 60, and was exactly double (114 as compared with 57) above 60. The mortality was a little higher in men than in women, which is explained by the absence of men who were on military service, these statistics applying exclusively to the civilian population.

In his Paris thesis on tuberculosis in Corsica, Serpaggi shows that in spite of the healthy climate tuberculosis is very prevalent, perhaps even more so than in many other French departments. He attributes the dissemination of the disease to three principal causes, namely, malaria, alcoholism, and consanguineous marriages. The whole of the sea-coast, especially on the east, as well as the neighbouring region up to an altitude of about 300 metres is infested by malaria, the recrudescence of which is probably due to the return of numerous soldiers who had contracted the disease in the east. Alcoholism, and especially the consumption of absinthe, is widely spread throughout Corsica, even in the smallest villages. According to Serpaggi, infection chiefly takes place in the school, where there is a complete absence of hygiene and no measures are taken to exclude tuberculous pupils. In some cases the families are infected by soldiers who have been discharged from the army for pulmonary tuberculosis. The disease also appears to be spread by milk and butcher's meat, there being no meat inspection except at Ajaccio and Bastia. Lastly, the large number of damp, dark, and generally insanitary houses is an additional cause of the prevalence of the disease in the island.

Aetiology. After admitting that there can be no tuberculosis without the tubercle bacillus, Lundborg produces numerous arguments in support of his hypothesis that the disease is largely an expression of degeneration of inferior quality determined by a too wide regrouping of the genotypical elements in the parents. Within certain limits consanguinity is a protection against degeneration and, other things being equal, the tuberculosis mortality will be found to be lowest in those countries with the most racially homogeneous population. Even in one and the same community, tuberculosis is most prevalent among the poorest classes, because in them mating is most indiscriminate, and the regrouping of the genotypical elements is widest. In the middle classes of the same community, mating is a more selective process and is kept within narrower limits. Lundborg reproduces a chart showing that the tuberculosis mortality in different European countries is directly proportional to their racial heterogeneity. Thus Poland has a high tuberculosis rate, while Iceland, where racial consanguinity has been kept pure through successive generations, remains comparatively immune. Among many other arguments in favour of his hypothesis, Lundborg refers to investigations carried out in 1885 in Norway by Uchermann. He found there were 1,826 cases of deaf-mutism, 932 of which were congenital. This congenital deaf-mutism was four times as common in consanguineous as in other marriages, but the mortality from pulmonary tuberculosis among the parents of these congenital deaf-mutes was only 14·5 per cent. as compared with 18 to 19 per cent. for all adults between the ages 21 and 60. Lundborg also applies his hypothesis to bovine tuberculosis, observing that purely home-bred stock exhibits a much lower tuberculosis morbidity than mixed stock.

Bovine tuberculosis. Schaeffer's investigations were prompted by certain alarmist reports as to the increase of bovine tuberculosis in human beings in Germany during the war. Thus Hart and Rabinowitsch published in 1917 a paper in which they maintained that during the first 2½ years of the war necropsies had shown a great increase in the incidence of primary intestinal tuberculosis. In 5 out of 6 such cases they isolated the bovine type of bacillus. Schaeffer's scrutiny of these investigations shows that they dealt with far too small a material to justify any dogmatic conclusions. Indeed, these authors appear to have found about a dozen cases sufficient for working out percentage estimates! Schaeffer's own figures are also small, but he finds that the combined evidence of post-mortem and clinical examinations shows no sign of a general increase of bovine infection. He has tackled the problem from another quarter by investigating the incidence of tuberculosis in cattle during the war as revealed by (*a*) meat inspection, and (*b*) notification of 'open' tuberculosis in cattle. He prefaces these investigations with the comment that as the cattle in Germany suffered great privations during the war and lived on little else but hay, straw, and a few potatoes and beet-roots, a notable increase of bovine tuberculosis might well be anticipated. But the statistics from both the sources referred to suggested that there was a decrease rather than an increase of bovine tuberculosis during the war. He found, however, that during the war precautionary measures against contamination of the milk with tubercle bacilli were appreciably relaxed. He contrasts this maintenance of the *status quo* of bovine tuberculosis with the enormous increase of human tuberculosis in Germany during the war.

Seifert, a veterinary surgeon in Dresden, has collected a mass of statistical information as to the distribution of bovine tuberculosis in practically every civilized country in the world. He finds that this disease is increasing and has become the most common of all diseases in cattle. According to the statistics of meat inspection in Germany, the incidence of bovine tuberculosis has steadily risen from 5 per cent. in 1888–89 to 23·5 per cent. in 1912. Within 8 years (1904–12) the disease has increased by 36 per cent. (from 17·3 per cent. to 23·5 per cent.). He quotes Haupt as saying that 60 per cent. of all cattle in Germany give a positive reaction to tuberculin. A similar rise is demonstrable in most other countries. In Vienna, meat inspection showed an incidence of only 1·4 per cent. in 1894, as compared with 2·5 per cent. in 1908–9, i. e. an increase of 79 per cent. in 15 years. The differences between the findings of meat inspection and the tuberculin test are often great; thus in Bohemia the former showed an incidence of only 2 to 2·5 per cent., whereas the latter showed as high a percentage as 15·1 to 18. Seifert concludes that bovine tuberculosis is intimately associated with intensive farming and the departure from the natural, primitive conditions of life. The disease is most prevalent in large farms into which cattle from other farms are frequently imported. Conversely, it is rare in small farms where the supply of cattle is maintained by home-breeding. In addition to infection, forced milk production, overcrowding, and feeding with refuse from industries, such as distilleries, breweries, and sugar factories, lower the vitality of the cattle. The disease is more prevalent in females than males, owing to the debilitating effects of forced milk production and calving—effects comparable with those of industrial employment in man. The part played by actual infection is stressed by the fact that the incidence of tuberculosis increases with age. Thus in more than half of all the cases of bovine tuberculosis the cattle are more than 6 years old.

Trauma and tuberculosis. Oliver's experience at a war hospital has been that in only an extremely small number of wounded soldiers has a relationship between gunshot wounds of the chest and tuberculosis been observed. Though unable to see how traumatism, *per se*, can produce a disease of the lungs so distinctly microbial as pulmonary tuberculosis, he admits that it may light up quiescent disease by liberating micro-organisms which are held up in the lungs or elsewhere, and that these may infect fresh ortions of the lungs or be carried to distant parts of the body. It is also possible that trauma, by reducing local and general resistance, creates a condition of soil favourable for the development of tubercle bacilli introduced from without.

Daguet maintains that before any causal connexion between a chest wound and pulmonary tuberculosis can be admitted the following conditions must be fulfilled: 1. The diagnosis of tuberculosis must be definitely established, and the disease must be in an active stage with tubercle bacilli in the sputum. 2. The pulmonary lesion must be situated on the same side as the wound, and as far as possible in the same region as the wound itself. 3. The onset of the tuberculous process should occur as soon as possible after the wound. Daguet records a case in which all these conditions were fulfilled. The patient was a soldier, aged 24, who received a penetrating shell wound in the anterior superior part of the left side of the thorax on September 28, 1918. The wound did not heal completely till April 15, 1919. The patient began to cough and lose flesh in February 1919. Examination in August 1919 showed active tuberculosis of the left apex and numerous tubercle bacilli in the sputum.

Conjugal tuberculosis. In an investigation which covered 1,000 successive dispensary cases, 502 of whom were married and 498 were single, Minnig, of Denver, found that there was active tuberculosis in husband and wife in 44 cases or 8·7 per cent. Of the 44 cases 22 of the consorts had died of tuberculosis. Of the 22 surviving, 17 were men and 5 women. Tubercle bacilli were present in 12 out of the 22 widows or widowers. The period of illness extended from four months to 20 years. Minnig maintains that in private practice the incidence of marital infection is smaller, proving that intelligent prophylaxis is worth while. (Cf. *Medical Science*, 1920, **2**, 227).

Morbid anatomy. Although the question as to which lung is most frequently affected by tuberculosis has been frequently discussed, comparatively few statistics on a large scale have been published, the most important being those of Strandgaard and Cavalcanti. Among 2,432 patients of Boserup Sanatorium Strandgaard found both lungs equally affected in 16 per cent., and in the rest the right lung principally or alone affected in 63 per cent., and the left in 37 per cent. Cavalcanti, who examined 800 cases at the Berg Sanatorium at Davos, found both lungs equally affected in 5·8 per cent., the right principally in 49·37 per cent., and the left in 44·75 per cent. Both writers concluded from their observations that the disease generally begins in the right apex and at first extends over the right lung, but that when the second stage is reached the disease remains stationary in the right lung, and advances more rapidly in the left, so that the left lower lobe is affected more frequently and severely than the right. Mayer, from whose paper the above information is taken, examined the first 2,500 cases of tuberculosis in Turban's sanatorium at Davos, and his results confirmed on the whole those of the previous observers. Mayer found that both lungs were equally affected in 1·36 per cent., the right lung principally affected in 50·56 per cent., and the left lung principally in 48·08 per cent. He attributes the predilection of the disease for the right lung to the defective aeration and circulation resulting from the asymmetrical ramification of the bronchi and blood-vessels in the three lobes of the right lung, and suggests that the rapid progress of the disease in the left lower lobe is due to obstruction to the circulation and respiration caused by the heart.

Blood. Asua concludes that there are two leucocyte pictures met with in the tuberculous. The first shows a normal total count, eosinophilia, lymphocytosis, and monocytosis. The Arneth count is normal or shifted to the right. This type is that of vagotonic individuals and is significant of successful resistance to the disease. Sympatheticotonic persons show the second formula, viz. increased total count, polynucleosis, total disappearance of eosinophils, and a shift of the Arneth count to the left. This is a defensive formula met with in virulent tuberculosis. Lymphocytosis and eosinophilia are the specific reactions of the organism to tuberculosis, and where these fail we are entitled to deduce that the resistance is very poor and the prognosis consequently bad. Asua believes that this is particularly apt to be the case in sympatheticotonia.

Hewat details a case which shows how important it may be to remember that in tuberculosis of other tissues there is a strong tendency to excess of lymphocytes, whereas in tuberculous meningitis there is a well-marked polymorph leucocytosis. In his case this reached 26,600 with 84 per cent. of polymorphs.

Symptomatology. Lawrason Brown and his colleagues at the Trudeau Sanatorium, Heise, Petroff, and Sampson, define clinical activity in pulmonary tuberculosis as 'that state in which pathological activity is not latent, but is producing, through the actual and immediate absorption of poisons, certain clinical or laboratory manifestations of disease, which disease may in turn be progressing, stationary, or even, for the time being, retrogressing'. Clinical activity, therefore, always implies pathological activity, but not *vice versa*.

Correlating laboratory findings with these ideas, they conclude that the presence of bacilli in the sputum indicates pathological activity in about 90 per cent. of all cases. A positive complement fixation reaction indicates pathological activity, but not necessarily, of course, in the organ under study. An attempt is made to define the stereoscopic X-ray shadows associated with pathological activity. In an area of active lung disease uncomplicated by scar tissue or calcification, the picture is that of a 'cotton-ball' appearance blending with a hazy surrounding area. Sometimes the shadows are more homogeneous, suggesting 'cotton batting'. If the disease retrogresses, the surrounding lung appears to become better aerated, and the 'cotton-ball' becomes smaller and more compact, or fades off to leave dotted or string-like shadows. In the stage of ultimate scar tissue the plates show either these wiry shadows or else dense discrete mottling, either isolated or conglomerate. Any hazy or cloudy fields show a clearly defined margin. If the disease progresses one sees multiplication rather than individual growth of the 'cotton-balls'.

Correlating clinical activity with signs and symptoms, the authors find that 90 per cent. of the relapsed have a positive complement fixation reaction, and 70 per cent. were clinically active cases. Only half the cases with bacilli *plus* râles prove to be clinically active, while of cases without bacilli there is clinical activity in 20 per cent. irrespective of whether râles are present or absent.

Duboff reports 20 cases of **tuberculous empyema**, half of which occurred in the course of therapeutic pneumothorax, preceded by definite symptoms of lung rupture. This is an accident to which a friable caseous cavern wall would seem to be particularly liable, when subjected to the strain of coughing and no longer supported by anything firmer than an elastic layer of air. The exudate is at first serous and lymphocytic, and at this stage guinea-pig inoculation is negative; but it rapidly becomes purulent, with polynuclear predominance, and, though guinea-pig inoculation may still occasionally be negative, bacilli can almost always be found. Of sixteen cases examined, bacilli were found in fourteen. Mixed infection is uncommon, at least without fistula formation. Even communication with a bronchus is no guarantee that mixed infection is present. Many of the cases were quite afebrile over long periods, and the general lung condition often showed some temporary improvement.

The author inclines to conservative treatment, but has had no experience of thoracoplasty. In the presence of pressure symptoms (pain, dyspnoea, irritable cough, &c.) aspiration should be done through a fine needle, followed by air replacement if, as is generally the case, it is desirable to keep the lung collapsed. When the chest refills rapidly, and fever and cachexia supervene, rib resection and drainage must be done.

Rosenthal's study of 157 cases of **haemoptysis,** observed between 1908 and 1918 at the Kommune Hospital at Copenhagen, has brought out the following points. In 84 to 85 per cent. the disease runs a benign course in spite of the haemoptysis, and in about 50 per cent. there is a history of symptoms suggesting that an exacerbation of the disease has preceded the haemoptysis. In this connexion Rosenthal argues that haemoptysis should be regarded rather as a consequence than a cause of exacerbations of the disease.

Edelmann and Hitzenberger, of the Vienna Medical University Clinic, state that in acute and subacute enlargement of the glands of the pulmonary hilus, such as occurs in incipient tuberculosis, pneumonia, whooping-cough, and acute bronchitis, tenderness of the spines of the second to the tenth dorsal vertebrae is present, a sign which E. Neisser in 1901 and J. Petruschky in 1903 regarded as characteristic of tuberculosis of the bronchial glands. But whereas the symptom is constant in tuberculosis, for a long time at least, in all the other diseases it rapidly disappears after subsidence of the primary disease. In the great majority of cases (49 out of 66) observed by Edelmann and Hitzenberger, which presented this symptom, an enlargement of the hilus shadow was shown by X-ray examination. They therefore regard this tenderness as one of the most reliable symptoms in acute and subacute diseases of the hilus glands, especially tuberculosis. They offer two explanations of the phenomenon. In the first place there may be a hyperaesthesia of the vertebral periosteum analogous to Head's areas in the skin. The other explanation, which is a purely mechanical one, is that percussion of the convex vertebral column produces waves of concussion which are transmitted to the glands lying in the centre of the convexity, and so produce pain just as shaking the bed does in peritonitis.

In his thesis on the asystolic forms of tuberculous **pericarditis** with effusion in the adult, Martin states that most writers are agreed that tuberculosis comes next to rheumatism as a cause of pericarditis, being responsible for about a quarter of all cases of pericarditis. The asystolic form appears to be fairly frequent, as in 43 cases of tuberculous pericarditis with effusion, which he collected from the literature, 8, or about one-fifth, showed symptoms of asystole, which may be explained either by mechanical obstruction to the circulation (compression of the right auricle) or by myocarditis. Martin distinguishes two varieties of the asystolic form of tuberculous pericardial effusion. In the first group the asystole is obvious from the onset of the affection, the patients presenting all the appearances of cardiac disease, while in the second group the asystole does not develop till late. The difficulties of diagnosis arise from the confusion which may exist between this form of asystole and that of chronic cardiac affections. Certain differential features, however, such as preservation of a regular cardiac rhythm, absence of venous pulsation, and a pulsus paradoxus are in favour of the diagnosis of pericardial effusion.

The condition may also be mistaken for adherent pericardium, the symptoms of which are almost identical. The tuberculous nature of the affection may be suspected from the almost invariable coexistence of tuberculous pleurisy or signs of pulmonary tuberculosis. Cytological examination may sometimes reveal the tuberculous origin of the effusion, but the puncture is often negative. Owing to the inefficiency of medical treatment the fluid should be evacuated either by puncture or pericardiotomy.

As the result of the examination of six cases of **phlebitis** which occurred in the last stage of pulmonary tuberculosis, Halbron and Paraf found that the tubercle bacillus was alone responsible for the appearance of the phlebitis. Secondary infection was excluded by the negative result of blood cultures, cultivation of the clot, and sections. On the other hand, tubercle bacilli were found in the blood and in the clot.

From the study of the **blood-pressure** in more than 700 cases of pulmonary tuberculosis, Marfan and Vannieuwenhuyse found that the systolic pressure was usually lowered. As a general rule the fall was all the more pronounced the more serious the case, and increased as the disease grew worse. In some cases, however, the systolic pressure was persistently normal or even raised. In these cases the disease was usually favourable, its course being either very slow or not progressive at all. While a normal or high blood-pressure was as a rule a good prognostic, a low tension did not exclude the possibility of improvement and even of clinical recovery, provided the fall was not too low. But while a favourable course was the rule in tuberculous patients with a normal or raised blood-pressure, in patients with low tension it was the exception. The writers insist that no conclusion can be drawn from a single measurement of the blood-pressure, and that the results can only be taken into account when the measurements have been repeated several times at more or less long intervals and under the same conditions. The diastolic pressure generally remains within the normal and only falls in the last stage. From a practical standpoint its determination is of less importance than that of the systolic blood-pressure.

De Bloeme examined the blood-pressure by the auscultatory method with Riva-Rocci's instrument in 500 cases of pulmonary tuberculosis and came to the following conclusions with regard to the diagnostic and prognostic value of sphygmomanometry in this disease. Cases with a systolic blood-pressure of 80–100 mm. Hg could be recognized by other diagnostic methods, and the estimation of the blood-pressure was merely confirmatory of other findings. Cases of this kind under the writer's observation died within 6 to 12 months, with the exception of a few patients who showed a reading of 90–100 mm. without any constitutional symptoms and were probably examples of essential hypotonus. The most important group consisted of men who had a blood-pressure of 100–110 mm., as in such cases the seriousness of the condition was more easily recognized by sphygmomanometry than by any other method. The most favourable cases were the patients of both sexes who had a blood-pressure of 110–150 mm. As regards individual cases the writer found that a patient with a low blood-pressure was more liable to a relapse than a patient with a normal reading, in spite of apparent improvement shown by increase in weight, diminution in the amount of sputum, and a normal temperature and pulse. Patients with a relapse showed a low blood-pressure even after the general and local symptoms had subsided. When considerable improvement took place, the blood-pressure rose. A definite fall of blood-pressure in an apparently slowly progressive case indicated a more unfavourable course than might otherwise be supposed.

Steven examined the blood-pressure of a large number of patients with surgical tuberculosis during heliotherapy and found that in almost all there was a fall of 10–20 mm. Hg during the treatment. In most cases the pressure fell directly after the beginning of the treatment and remained at more or less the same level during the following hours. In the evening it returned to its usual height or slightly exceeded it. The fall of blood-pressure was readily explained by the hyperaemia of the skin caused by the sun's rays with subsequent reduction of the pressure in the internal vessels. It was also conceivable that the vascular system as a whole was affected and that a reduction of tension took place from the vasomotor centre. As a rule the fall of blood-pressure was accompanied by an increased pulse frequency. Steven therefore recommends that in a patient whose heart possesses little reserve power heliotherapy should be employed with caution.

Nauclér's contribution to the study of the blood-pressure in pulmonary tuberculosis includes an exhaustive review of the literature and original work carried out in a hospital 40 metres above sea-level. The measurements were made during the patients' rest hour, between 3 and 4 p.m., in the recumbent position. The Riva-Rocci-Recklinghausen apparatus was used with a 13 cm. wide cuff embracing the middle of the forearm held at the level of the heart. The systolic as well as the diastolic pressure was measured according to Korotkov's method. The number of the patients was: 65 men, 44 women, and 90 children between the ages 6 and 15. Although there were considerable individual differences, the average blood-pressure was highest in the early stages of the disease, lowest in the last stages. In 60 per cent. of the patients in Turban's first class the pressure was below normal. There were therefore several early cases in which the pressure was normal or higher, and a low pressure cannot accordingly be accepted as a reliable sign of early phthisis. The pressure was more dependent on the severity than on the extent of the disease, and the lowest pressures (80 to 89 mm. of mercury) were noted in moribund cases. The fall of pressure was often most abrupt when, at the first measurement, it was fairly high. The fall was less steep when the pressure was already low. The pressures were highest in cases gaining weight, lowest in cases losing weight; the height of the pressure was directly proportional to the severity of a reaction to an intracutaneous injection of tuberculin. A definite relationship was also established between both the frequency and the severity of haemoptysis and the height of the blood-pressure.

Kieffer's investigations at the Municipal Hospital for diseases of the lungs in Mannheim, in the period 1912–19, have convinced him that **intestinal tuberculosis** is a very frequent and serious complication of pulmonary tuberculosis. In 452, or 72 per cent., of the 629 cases of pulmonary tuberculosis examined *post mortem* he found signs of intestinal tuberculosis. In about half these cases there had been no symptom of intestinal disease before death. But when there were symptoms referable to the intestines death usually followed soon, and only 53 patients with signs of intestinal tuberculosis had left the hospital alive. In about one-third of the cases of tuberculosis of the intestines examined *post mortem* the disease was limited to a few nodules or isolated ulcers. The clinical course seemed largely to depend on the existence of secondary infection, and the higher up the disease was situated in the intestines the more severe and rapidly fatal was its course. Severe constipation occurring in conjunction with pulmonary tuberculosis was found to be a very reliable sign of intestinal tuberculosis. Occult haemorrhage was another important sign which was seldom absent. But such symptoms as pain, which depended on involvement of the peritoneum, were often lacking. Kieffer was repeatedly astonished by finding the peritoneum perfectly intact in spite of severe tuberculous disease of the intestines. Only in 10 out of a total of 2,312 cases did perforation of the intestines by tuberculous ulcers occur. The effect of the war was not only to increase the frequency of intestinal tuberculosis to double the pre-war rate, but also to make the course of the individual case much more rapidly fatal than before.

According to Mouisset **involvement of the liver** is frequent in tuberculosis. Histological examination very often shows the presence of tubercles in the liver, but the usual lesions are cirrhosis and steatosis. There is no doubt that tuberculous infection alone can produce these lesions, but the possibility of other aetiological factors must not be forgotten. On the other hand, it is not uncommon for the autopsy to show very pronounced lesions of hepatic cirrhosis in tuberculous patients who have never shown any clinical evidence of it during life, such as ascites or a collateral venous circulation. Mouisset has found that tuberculous patients who did present symptoms were almost always alcoholic. He therefore concludes that though cirrhosis of the liver is frequent in tuberculosis, it is usually latent in the absence of alcoholism. An exclusively tuberculous cirrhosis is chiefly of pathological interest, whereas the clinical picture of cirrhosis indicates the coexistence of alcoholism.

Ameuille records two cases in which jaundice appeared in the last stages of pulmonary tuberculosis. The jaundice was deep in one and slight in the other. The faeces were not completely colourless, but there was an abundance of bile-salts and pigment in the serum and urine and a little urobilin. At the autopsy no obstruction of the extrahepatic bile-ducts was found, and there was no naked-eye change in the intrahepatic bile-ducts, but on histological examination there was extensive fatty degeneration associated in one case with amyloid degeneration.

According to Massias, of Badcaux, **concurrent tuberculosis of the kidneys and suprarenals** is an uncommon event and may assume one of two forms, of each of which he records an example. In the first form the patient presents the complete picture of Addison's disease which proves fatal, and *post mortem*, in addition to caseous tuberculosis of both suprarenals, there is a closed parenchymatous renal tuberculosis which has been latent during life. In the second form coexistent tuberculosis of the kidneys and suprarenals is recognized during life, Addison's disease being associated with open renal tuberculosis, as shown by pyuria and the presence of tubercle bacilli in the urine. Massias thinks it probable that many of these cases of concurrent renal and suprarenal tuberculosis originate from infection of the lymphatic glands, as in most of the cases the aortic, biliary, and mesenteric glands are tuberculous. The gravity of the condition is mainly due to the suprarenal lesion, which can only be cured by the production of fibrosis, though, like the primary lesion, this may give rise to chronic suprarenal insufficiency. Nephrectomy is contra-indicated in such cases, and only the general methods of treatment for tuberculosis can be employed together with suprarenal opotherapy.

His comprehensive survey of the literature and his own investigations at the Pathological Institute in Christiania have led Harbitz to conclude that a considerable proportion of cases of definite **tuberculous meningitis** terminate in complete recovery. A comparison of fatal with non-fatal cases showed that the latter were often cases in which the patient had already exhibited signs of chronic, comparatively benign tuberculosis. Another point, brought out by this comparison, was the age of the patients in the two classes. It appears that 60 per cent. of all cases of tuberculous meningitis occur within the first 2 years of life, when the disease is invariably fatal. The proportion of recoveries increases with the age of the patient. No fewer than 12 out of 29 cases collected by Bókay in 1914 referred to patients between the ages 16 and 44. A comparison of the recoveries from epidemic cerebrospinal meningitis with the recoveries from tuberculous meningitis showed that the former are often incomplete, a chronic meningo-encephalitic condition with internal hydrocephalus and psychic changes supervening. The subjects of tuberculous meningitis, on the other hand, provided they survive the acute phase of the disease, recover completely as a rule, even when there have been definite anatomical lesions.

According to Hollis and Pardee, who report two undoubted and two doubtful cases in adults, there are 38 cases of tuberculous meningitis on record ending in recovery in which the diagnosis was certain, and 15 in which it was doubtful. Hollis and Pardee attribute the cure of their cases to intrathecal injections of antimeningococcal serum combined with frequent spinal drainage.

Barber reports a case of complete recovery from tuberculous meningitis in a woman aged 37, from whom a tuberculous kidney had been removed 12 years previously. Lumbar puncture was not performed until the fourth week from the onset, and was repeated in the fifth, sixth, and eighth weeks. The cerebrospinal fluid was under pressure, appeared clear, and contained a few lymphocytes and tubercle bacilli. The febrile period lasted fourteen weeks. On discharge from hospital in the twenty-eighth week the patient was well in every way.

Étienne records a case of tuberculous meningitis in a man treated by lumbar puncture and intrathecal injection of Vallée's antituberculous serum. Although death ultimately occurred, the results were encouraging. Decided improvement followed the injection at first, but the most striking results were (1) the disappearance of the tubercle bacilli from the cerebrospinal fluid, (2) the diminution of the meningeal reaction shown by the progressive fall in the number of the lymphocytes (from 8 to 4), and in the albumin content (from 0·80 to normal) of the cerebrospinal fluid.

In a paper on curable tuberculous meningitis in the course of chronic pulmonary tuberculosis, De Massary and Lechelle record the case of a woman aged 23, the subject of pulmonary tuberculosis, who developed signs of meningitis in October 1919. The cerebrospinal fluid showed lymphocytosis, excess of albumin, and two acid-fast bacilli. Gradual improvement took place and the patient was discharged in December. When seen again, in January and March 1920, she showed no signs of meningitis. The writers also allude to two other cases of tuberculous meningitis in which there was a similar meningeal manifestation a few months to a year previously.

Giroux reports two cases of tuberculous meningitis in adults in whom the cerebrospinal fluid obtained by lumbar puncture showed neither lymphocytosis nor excess of albumin. Similar examples of this rare condition have been recorded by Lackowicz (1901), Villaret and Tixier (1905), and Bernard (1901).

Genoese examined the cerebrospinal fluid of 23 cases of tuberculous meningitis for acetone, and, with four exceptions in which it was negative, found an intense reaction with Ricci and Frommer's tests. The urine in each of the 23 cases showed a large quantity of acetone, except in 3 cases in which the reaction for acetone was weak. In these 3 cases the cerebrospinal fluid also showed no acetone.

Dautrebande has examined 100 cases of pulmonary tuberculosis for the **myotonic reaction** described by Loeper, Lévy, Halbron, and others (vide *Medical Science*, 1920, **2**, 233), and comes to the conclusion that, though it may be found in a great variety of diseases, it is constant in pulmonary tuberculosis, in which it serves as a guide to the localization, extent, and activity of the lesions. A positive reaction in the pectoral muscles indicates a more extensive lesion than a positive reaction in the trapezius, and a positive reaction obtained by percussion of the clavicle and sternum is evidence of a more advanced lesion than a reaction obtained by pinching the axilla. Lastly, the muscular wave indicates lesions which are not found by auscultation, but are revealed by radioscopy. Investigation of the muscular wave should therefore form part of the examination of every patient suspected to be suffering from pulmonary tuberculosis.

According to Findlay, **tuberculous rheumatism,** which was first described by Poncet and Leriche, may be either primary or secondary, according as the joint manifestations precede or follow the development or, at least, the clinical appearance of visceral tuberculosis. The secondary variety does not differ in its symptomatology from the primary form, but its association with definite tuberculous lesions leaves no doubt as to its nature. The primary variety, on the other hand, may so closely simulate ordinary rheumatic fever that for a time its true nature may not be recognized. The condition may completely resolve, when the case will, in all probability, be regarded as one of rheumatic fever. Not unfrequently, however, gross visceral tuberculosis develops immediately or some time later, and thus enables a correct diagnosis to be made. Findlay records three illustrative cases in children. In the first the diagnosis made during life was rheumatic fever followed by pericarditis, pleurisy, and finally meningitis. The tuberculous nature of the disease was revealed by the autopsy. In the second case the rheumatic manifestations were followed by involvement of the lymphatic glands, pericarditis, and peritonitis. In the third case severe pains in the hips, knee, ankle, shoulder, elbow, and wrist-joints, without swelling, preceded the appearance of tuberculous adenitis.

Skin. During the past 10 years Haug has collected 13 cases of erythema nodosum which he has investigated with a view to establishing a connexion between this disease and tuberculosis. In nine cases the patients were tuberculous, exposed to massive infection, or they exhibited such ominous signs as pleurisy. Two cases were particularly instructive, as the patients, aged 15 and 18 respectively, came of healthy stock and developed erythema nodosum within three months of exposure to massive infection with tuberculosis. In three cases no connexion between the rash and tuberculosis, either in the patient or in 'contacts', could be established. One patient developed acute articular rheumatism of a month's duration immediately after the outbreak of erythema nodosum.

Gendron, of Nantes, reports an outbreak of three cases of erythema nodosum and one case of a miliarial eruption in a tuberculous family. The cases confirm the view that tuberculosis creates a favourable soil for the development of erythema nodosum, and point to the existence of an epidemic and contagious form of erythema nodosum resembling an eruptive fever. They also suggest that the incubation period is four days, and that miliaria may constitute a variety of epidemic erythema nodosum.

Gargiulo describes a special skin sign in patients with pulmonary or intestinal tuberculosis consisting in a roughness of the skin of the forearms, especially near the wrists and along the shafts of the radius and ulna. This roughness is in sharp contrast with the flaccidity of the skin present on the rest of the body, especially in women. Gargiulo who has found the sign present in 90 per cent. of his patients attributes it to the fact that wasting affects the forearm in preference to other regions. Profuse sweating is also a contributing factor, and it is not improbable that there are neurotrophic and vasomotor changes in the skin due to tuberculous toxins.

Tuberculosis and pregnancy. According to Dantier, who records several illustrative cases, pregnancy occurring in old cases of tuberculosis with slight lesions which have undergone fibrosis does not have any unfavourable influence on these lesions. On the other hand, it causes a considerable aggravation of active ulcero-caseous lesions, especially during the puerperium, when a rapidly fatal broncho-pneumonia or miliary tuberculosis develops in the great majority of cases. Pregnancy, and especially delivery, may give rise to subacute tuberculosis manifestations, such as pleurisy or pleuro-pulmonary congestion in women who have hitherto been clinically free from tuberculosis. A state of tuberculin anergy is caused by pregnancy, and still more so by the puerperium, as is shown by the disappearance or diminution of the cuti-reaction towards the end of pregnancy or from the second to tenth day *post partum*. This anergic state may serve to explain the disastrous effect of the puerperium on the course of pulmonary tuberculosis.

Tuberculosis and acute infections. In a paper on the capability of reaction in pulmonary tuberculosis Országh alludes to an outbreak of 36 cases of tonsillitis and 86 cases of vaccination in the Queen Elizabeth Sanatorium at Buda-Pesth to show that the condition of the tuberculosis patients was not unfavourably affected either by the attack of tonsillitis or by vaccination. The severer the attack of tuberculosis the less likely was the patient to contract tonsillitis or for the vaccination to be successful. Mild cases of tuberculosis showed the same reactions as normal individuals, and the power of reactions diminished or disappeared in the advanced third stage as is the rule in some chronic diseases (cf. *Medical Science*, 1919, **1**, 161).

Tuberculosis and Graves's disease. Galotti, of Brescia, reports six cases of pulmonary tuberculosis presenting a more or less complete picture of Graves's disease. His conclusions are as follows: (1) Symptoms of Graves's disease not unfrequently accompany pulmonary tuberculosis both at the onset and throughout its course. (2) In many cases the symptoms of

Graves's disease may be regarded as a probable symptom of latent pulmonary tuberculosis. (3) Enlargement of the thyroid often complicates tuberculosis, to which it imparts a characteristic mild course. (4) In cases of pulmonary tuberculosis complicated by Graves's disease, treatment of the thyroid gland may have a favourable effect on the pulmonary disease and soon cure it.

Immunity. As the result of an inquiry of 49 companies in which the men were habitually exposed to sulphur dioxide or the fumes of sulphuric acid, Tweddell found that the percentage of tuberculosis among workers was negligible. Sulphur dioxide and sulphuric acid appeared to act as preventatives of tuberculosis and perhaps as a cure, with the possible exception of fibroid phthisis.

Diagnosis. In an article on pulmonary tuberculosis in soldiers and and prisoners of war, Boeri, professor of medicine at the University of Cagliari, in Sardinia, remarks that the lessons to be learnt from so-called war medicine are also applicable to the medicine of civil life. The investigation of tuberculosis in soldiers and prisoners of war has shown the necessity of not confining one's attention to signs of active or suspected tuberculosis, but also of extending it to those predisposed to tuberculosis. In addition to the ordinary criteria Boeri describes the following: (*a*) Morphological criteria, which include the vertical or drop-heart, often associated with a floating or mobile tenth rib, or with a mobile ninth rib and splanchnoptosis; (*b*) a functional criterium comprising atony, neuromuscular asthenia, dyspepsia, suprarenal insufficiency, low blood-pressure, tachycardia, &c.; (*c*) the criterium of morbid sensibility of the respiratory system, shown by bronchial debility (François and Flurin, Florand), respiratory claudication (Labbé and Arce), and respiratory weakness of the pulmonary apex. In the recognition of latent or initial tuberculosis Boeri attaches importance to hypotrophy of the outer border of the trapezius, atrophy of the sternomastoid on the affected side, and to hypertrophy of the sternomastoid on the healthy side.

He maintains that amyotrophies such as depression of the thorax and limitation of the respiratory movements in pulmonary tuberculosis are not the sequelae but rather the accompaniment of the process in the lungs, of which they are often the early signs, being due to a neurotrophic reflex between the lung and the respiratory muscles.

In addition to other well-known affections of the apex of a non-tuberculous nature which have to be distinguished from pulmonary tuberculosis, Boeri mentions the apical localization of Malta fever, bronchitis and bronchopneumonia, and echinococcus cysts, which are prevalent in Sardinia, where they are not always easy to recognize, especially in the form associated with haemoptysis. Respiratory complications of malaria are also apt to be mistaken for tuberculosis, especially in Sardinia, but may be recognized by the predominance of auscultatory over percussion signs, their short course, the disproportion between the general disturbance, especially high fever, and the local signs, and by the action of quinine. In respiratory affections simulating tuberculosis the physical signs shift within a short space of time from one part of the chest to the other, whereas in tuberculosis the same signs tend to remain in the same situation.

During the past two years Helms has employed the X-rays for diagnosis in every first stage case admitted to his sanatorium without tubercle bacilli in the sputum and with indefinite stethoscopic signs. The X-ray evidence coincided with that of the stethoscopic examination in 66 cases. In

17 cases the X-rays showed more than the stethoscopic examination, in 10 cases less. In 51 cases in which no adventitious sounds could be heard, the X-ray evidence was also indefinite. Helms remarks that several patients are admitted to sanatoriums without tubercle bacilli in the sputum, with indefinite stethoscopic signs, and with only a vague history of symptoms. Such patients should be discharged at once if the X-rays show no sign of recent pulmonary tuberculosis or of hilus tuberculosis. On the other hand if the history is suggestive of pulmonary tuberculosis, and the X-ray signs are positive, sanatorium treatment should be given even in the absence of stethoscopic signs and of tubercle bacilli. No case of doubtful pulmonary tuberculosis should be regarded as adequately investigated without an X-ray examination.

Pritchard and Roderick investigated the **complement-fixation test** for tuberculosis in 466 cases, 220 of which were pulmonary tuberculosis, including suspects, 13 extra-pulmonary tuberculosis and 233 non-tuberculous, and come to the following conclusions. The reaction does not give such valuable and constant information as the Wassermann reaction in regard to syphilis. In some open advanced cases of pulmonary tuberculosis no reaction occurred. This the writers attribute to the cells having lost their power of reaction owing to prolonged saturation with specific toxins. The test was of greatest help in differential diagnosis. It also acted as a stimulus to more careful clinical observations (cf. *Medical Science,* 1920, **2**, 237, 282).

Pestalozza, of the Milan Paediatric Clinic, states that in 1916 Pisani suggested performing the **cuti-reaction** at the site of the tuberculous focus instead of on the arm, as is generally done, as he had observed that the reaction was usually more intense in the skin over the affected organ than on the corresponding region on the opposite side or on the arm, and in many cases the reaction was positive over the diseased area and negative in the arm. In 1918 Pollitzer studied the regional cuti-reaction in 40 children aged from 2 to 9 years, and came to the conclusion that the cuti-reaction over tuberculous focus was almost always more intense than that made on the healthy part on the opposite side or on indifferent regions such as the arm. In 75 cases in which the cuti-reaction was performed still more recently by Da Gradi in adults, after subtracting 24 cases in which the cuti-reaction was negative both over the tuberculous focus and at a distance therefrom, in 17 of the remaining 51 the cuti-reaction was positive at the focus and negative in the arm, and in 34 it was positive both at the focus and in the arm, but was often more intense at the focus. Pestalozza himself performed the regional cuti-reaction in 72 cases, using human tuberculin on the right arm, bovine tuberculin on the left arm, and both tuberculins over the tuberculous focus about 4 cm. distance from one another. In 27 cases the reaction was negative both over the focus supposed to be tuberculous and on the arm. In the other cases, though the regional cuti-reaction was often more intensely positive than that performed at a distance from the focus, in none of the cases was the regional reaction positive and the other reaction negative. This result deprives the test of much of the practical value which the regional cuti-reaction appears to have in the case of adults.

Fine states that the von Pirquet test has been employed by the Newark Board of Health during the last two years in 1,530 children from tuberculous families, i. e. families in which one or two members had active tuberculosis, with the following results: von Pirquet positive, physical examination negative, 344 cases, or 21 per cent.; von Pirquet negative, physical examination negative, 798 cases, or 52·1 per cent.; von Pirquet positive, physical examination positive, 376 cases, or 24·6 per cent.; von Pirquet negative, physical examination positive, 12 cases, or 0·08 per cent. This shows that 45·5 per cent. of the total number of children examined gave a positive von Pirquet reaction, and that 52·9 per cent. of those with a positive reaction had signs of tuberculosis in the chest, while 52·9 per cent. of all examined gave a negative von Pirquet reaction, and of these only 1·4 per cent. showed physical signs in the chest.

Synwoldt, of the Rostock University Medical Clinic, made comparative observations with human and bovine tuberculin cutaneous tests, and found that bovine tuberculin was more sensitive both from a diagnostic and prognostic standpoint than human tuberculin. Thus, in a group of 39 children with a family and personal history of tuberculosis, but without any physical signs, 5·12 per cent. gave positive reactions with both human and bovine tuberculin, 76·93 per cent. were negative with both reactions, and 17·95 per cent. were negative with human and positive with bovine tuberculin. In another group of 18 cases in the third stage of pulmonary tuberculosis 12 cases were negative with bovine reactions and 6 were positive with bovine and negative with human tuberculin. The course of the disease in these 6 cases was relatively favourable and suggested that they still possessed antibodies capable of resistance. Synwoldt concludes that the use of the bovine tuberculin reaction in addition to the ordinary old tuberculin reaction represents a considerable progress both from the diagnostic and prognostic point of view.

Hilgers and Gentzen performed tuberculin tests on 100 children belonging to a middle-class girls' school at Königsberg and found that 65 per cent. gave a positive reaction with von Pirquet's test and 15 of the remainder gave a positive Hamburger's *stich* reaction. 20 children gave no reaction with either method, so that a positive result was obtained in 80 per cent. The writers recommend that similar observations should be made in schools in the country.

In the course of a long series of investigations into the effects of the war on the development of school children in Stockholm, Kjerrulf carried out v. Pirquet's test, distinguishing between the first-born and the later-born. In one school with 1,831 pupils the reaction was positive in 26·4 per cent., and this ratio was exactly the same for the first as for the later-born.

Lawrason Brown and Heise have collected the 324 cases in which diagnostic subcutaneous injections of Koch's old tuberculin were given at the Trudeau Sanatorium during the last 24 years. In 42 cases no reaction was obtained to a second injection of 0·01 c.c. or 10 mg. of O.T., and none of these cases was known to have terminated fatally from pulmonary tuberculosis. Patients who fail to react to this dose may, therefore, be safely discharged from a sanatorium. With regard to the significance of a positive reaction, the writers suggest that when it is accompanied by a definite focal pulmonary reaction, as shown by the X-rays, it is probably the wiser course to recommend sanatorium treatment for three to six months even if other evidence of active tuberculosis is inconclusive. The X-ray picture, which they interpret as indicating a focal pulmonary reaction, is a cottony, hazy appearance about a previously sharply defined 'dense' nodule. This condition, which disappears after some days, may be interpreted as a congestive process. Given with knowledge and discretion, tuberculin produces no lasting untoward results, and even the temporary effect may be beneficial.

Treatment. Saugman's investigations into the fate of patients discharged from his sanatorium in the period 1900–17 show that the prognosis for patients who can afford treatment in a private sanatorium is comparatively good. All but 164 of the 2,360 patients were traced; 44·9 per cent. were in 1920 still fit for ordinary or light work, 42·5 per cent. had died of tuberculosis, and 2·8 per cent. of other diseases. Among the first stage patients 78·6 per cent. were still fit for ordinary or light work. The corresponding percentages for the second and third stage patients were 73·6 and 27 respectively. Saugman concludes from these figures that in 8 or 9 out of every 10 cases admitted to a sanatorium in the first stage of the disease, complete and permanent arrest can be effected. Of second stage patients, two-thirds may expect to be fit for work 15 years after discharge, and a quarter of all third stage patients may expect to be fit for work 10 years after discharge, or one-fifth 15 years after discharge.

In connexion with the advocacy by certain physicians in Denmark of short spells of sanatorium treatment instead of longer periods, Ostenfeld has investigated the fate of the 1,496 patients treated at the Faksinge working-class sanatorium for men in the period 1908–14. The fate of 1,278 of these patients was investigated 5 years or more after discharge. It was found that 44 per cent. of these 1,278 patients were still fit for whole- or part-time work. Yet the disease was in most cases advanced; 19·8 per cent. belonged to the first stage, 25·6 per cent. to the second stage, and 54·7 per cent. to the third stage of the disease. Five years or more after discharge, 76 per cent. of the first stage cases were still fit for whole-time work, and another 6 per cent. for part-time work. The proportion of patients fit for whole-time work in the second and third stages of the disease were 51 and 18·5 per cent. respectively. In each of these stages there was another 6 per cent. still fit for light work. Ostenfeld attributes these comparatively good results to the principle adopted at his sanatorium of prolonging residence according to the needs of the individual case instead of limiting it to a standard period. The average duration of treatment for patients with positive sputa was 153 days for the first stage, 199 days for the second stage, and 214 for the third stage of the disease. The residence of patients with negative sputa was appreciably shorter. As Ostenfeld's figures show, the prognosis for patients whose sputa become negative under sanatorium treatment is practically as good as for those first and second stage patients in whose sputa tubercle bacilli have never been found. Hence the wisdom of prolonging sanatorium treatment till sputa have become negative. Ostenfeld also notes the comparative frequency with which patients remain fit for work although their sputa contain tubercle bacilli on discharge. Among second stage patients, 32 out of 94 with positive sputa were still fit for work 5 years after discharge.

Criticizing the statisticians who attempt to prove that sanatoria are useless, Paterson points out that working-class patients who achieve a cure are often lost sight of, whereas patients who relapse report themselves for further treatment. He calculates that, if patients are given sanatorium treatment before their resistance has broken down, permanent results may be obtained in about 80 per cent.

Rutledge and Crouch have conducted inquiries into the after-histories of 1,654 patients discharged from the Modern Woodmen of America Sanatorium 4 to 9 years earlier. They found that 771, or 46·6 per cent., were still alive, and 883, or 53·4 per cent., were dead. In 1,229 of the 1,654 cases tubercle bacilli were found in the sputum. Of these sputum-positive cases, 33·6 per cent. were living and 66·4 per cent. were dead. The writers conclude that the moderately advanced case with bacilli in the sputum has an even chance of living for 5 years after discharge from a sanatorium. They note that more than one-half of the deaths among the sputum-negative cases were due to non-tuberculous causes.

From observations on food values at the Gateforth Sanatorium, Leeds, Woodcock and Ruston have come to the following conclusions: (1) Tuberculous patients require more food than the average amount needed by the ordinary labourer outside. The minimum for the Gateforth patients is 3,500 calories, the patients being almost invariably adults. (2) The diet must be rich in protein and fat. The fat should be largely animal fat in the form of milk and milk products. (3) Eggs should be included in the dietary, or their place should be taken by an extra amount of meat given according to accurate calculation. (4) Whole-meal bread, beans, peas, and lentils should always be used, together with a plentiful supply of fresh fruit and vegetables grown in the sanatorium grounds. (5) Two pints of milk a day should be given to each patient.

Proteintherapy in the form of subcutaneous injections of normal horse-serum was employed by Czerny and Eliasberg in 26 cases of tuberculous cachexia at the Berlin University Children's Clinique, from ½–2 c.c. being given daily. The treatment appeared to have a favourable effect on the general condition and also to cause a change in the reaction to tuberculin, a torpid reaction or admission being converted into a normal reaction.

Unlike Schmidt and Kraus, who claim to have obtained as good results by injections of milk in the treatment of pulmonary tuberculosis as by injections of tuberculin, Lewin, who used injections of milk in 25 cases, did not see any distinct success in a single one, and concludes that the method cannot be substituted for tuberculin in the treatment of pulmonary tuberculosis.

Borgogno, director of the Anti-tuberculosis Dispensary of Alessandria, has made an extensive use of Spengler's immune bodies and has come to the conclusion that they have no effect in severe forms of open tuberculosis with pronounced toxaemic manifestions. On the other hand, he found that they were beneficial in apyrexial forms of tuberculosis and most effective in the pre-tuberculous or in the initial stage of tuberculosis in which symptoms due to tuberculous toxins dominate the clinical picture.

Krysolgan, which was introduced by Spiess and Feldt in 1917, is a sodium salt of *p*-amino-*o*-aurophenol carbonic acid. It is easily soluble in water, gives a neutral reaction, and contains about 50 per cent. of gold. Reviewing his clinical experiences of this drug, Geszti does not attempt a statistical analysis, but gives very full details of 9 cases, adding that he has treated 25 to 30 other patients with this preparation. He is greatly impressed by its action, which corresponds rather with that of tuberculin than with that of the modern drugs of chemo-therapy. But while tuberculin produces a focal reaction which may lead to permanent damage and extension of the disease, the focal reaction to krysolgan invariably proved beneficial, being followed by signs of repair. This focal reaction appears to be provoked by the deposit of gold in the diseased area for which it has a selective action. Recent disease reacts more favourably to this treatment than chronic fibrotic disease, because in the former case the circulatory conditions facilitate the permeation of the drug and its deposition in the affected tissues. Its affinity for tuberculous tissues is not the biological affinity of tuberculin, but appears to be dependent on anatomical factors. Geszti assumes that the circulation in tuberculous foci is such that the drug gains easy access to it, but does not escape as easily, and is, therefore, deposited. The drug does not fulfil Ehrlich's stipulation that a chemo-therapeutic remedy must possess high bacteriotropic and low organotropic properties. Indeed, it would seem that the beneficial action of krysolgan depends on its organotropic properties, which help to provoke a focal reaction, setting free antigens which stimulate the formation of antibodies. Without a focal reaction the effect of krysolgan is practically negative, and the gradual immunity to the drug achieved by successive injections is probably due to the fibrosis it sets up, gradually cutting off the drug from contact with the diseased tissues. Geszti gives 5 cg. of the drug dissolved in 5 to 10 c.c. of sterile, distilled water, injecting it into a vein of the arm. This dose is repeated at intervals of about 8 to 10 days when the reaction to the previous injection has passed off. The dose is gradually raised to 10 to 20 cg.; the absence of a reaction being taken as an indication for increasing the dosage.

At the St. Blasien Sanatorium, Rickmann has given krysolgan in 25 cases of pulmonary tuberculosis, 15 of which were complicated by tuberculosis of the larynx. The remaining 10 cases were of a slowly progressive character which did not react satisfactorily to ordinary sanatorium treatment. After giving details of several cases, Rickmann sums up his views thus. Krysolgan provokes an objectively demonstrable reaction which is often followed by signs of healing in both larynx and lungs. Combined with other methods it achieves results which these other methods by themselves cannot effect. The reaction may be so severe as to prevent the treatment being continued. Rickmann has seen violent intestinal catarrh and severe injury to the kidneys follow the exhibition of this drug.

Colbert and Bazin state that the differences in opinion as to the value of emetin in tuberculous haemoptysis are due to the fact that the drug is only active in cases of hypertension and occasionally in cases of low tension when the haemoptysis is accompanied by a rise of blood-pressure. Waller's experiment has shown that the most favourable conditions for haemostasis consist in arterial vasoconstriction with diminution of the energy of the heart-beart. The writers found that emetin acts on the maximum and minimum arterial pressure and on the oscillometric index. Treatment consists of an intramuscular injection of 0·04 grm. emetin repeated once or twice a day. As soon as the blood-pressure falls, the dose is reduced, but the drug should not be discontinued too soon. A purgative in the form of sodium sulphate should be given every morning, and the diet restricted. Adrenalin and horse-serum, which often raise the blood-pressure, should be avoided. If the temperature is too high, small doses of antipyrin may be given, as this drug has also a hypotensive action.

So far from accepting Bang's teaching, that immobilization and morphin are unnecessary and even harmful, Rosenthal cleaves to the tradition of absolute rest in bed, with morphin, ice-bags, and other time-honoured remedies. In support of this standpoint he shows that the average duration of the haemorrhages among his cases was considerably less than that among Bang's cases; between 40 and 50 per cent. of Rosenthal's cases responded rapidly to treatment, the haemorrhage being completely arrested within 4 days. Rosenthal has found the action of *acetas plumbicus* and *pulv. fol. digitalis* very prompt and reliable; he gives 10 cg. of each 5 times a day for about 4 or 5 days, withholding them when nausea is provoked or the haemorrhage is arrested.

Riviere calls attention to some points in connexion with the **artificial pneumothorax** treatment of pulmonary tuberculosis. With regard to the vexed question of the degree of unilaterality of disease which it is desirable to demand before having recourse to this treatment, he lays down the following criteria: (1) that one lung is so much diseased that its recovery under any known treatment while in an expanded and functioning state is despaired of, and (2) that the other lung is a fairly good organ and not the seat of active tubercle. The great majority of cases satisfying these demands Riviere recognizes as cases of hilus distribution.

With regard to the conduct of the operation, disintoxication should be the first aim in the early days of a therapeutic collapse. Where the other lung is a source of anxiety, the operator should be content at first with a moderate amount of collapse, with small fills at rather frequent intervals. The author warns against mediastinal overstretching and ballooning of the pleura, and describes an asthmatic condition suggestive of bronchial obstruction associated with the former. Lowering of pressure should in all cases be controlled by X-rays.

Discussing pleural effusion, Riviere refers to the danger of the lung creeping out and becoming attached below the level of the fluid. On account of this danger, and also that of excessive pleural thickening, he is loath to leave untapped an effusion which reaches half-way up the chest, and which has become stationary. Replacement should be done, air or nitrogen being admitted all the time that the fluid is flowing out.

Crocket states that since it was adopted five years ago artificial pneumothorax has been performed at the Consumption Sanatoria of Scotland, Bridge of Weir, in 80 cases, practically all of whom were in a hopeless condition at the time. In 12 the operation was successful, in 30 partially successful, and in 38 a failure. In the successful cases the temperature became normal, the cough and sputum entirely ceased, the weight increased, and the working capacity was to a fair degree restored. The causes of the limited success in the second group were (1) adhesions preventing entire collapse; (2) extensive diseases in both lungs; (3) bronchitis affecting the sound lung and recurring from time to time when weather conditions were unfavourable; (4) onset of influenza causing extension of the disease in the sound lung; (5) stopping the injections at too early a stage, reinduction being impossible on account of adhesions; (6) patient refusing further injections. Apart from its curative value, Crocket found the operation of great service symptomatically, as it relieved pleuritic pain, kept the cough in check, reduced the sense of fatigue, and frequently lessened the dyspnoea.

Fernandez reports on 50 cases of pulmonary tuberculosis that were subjected to artificial pneumothorax at the Leeds City Seacroft Sanatorium during the period of 18 months from September 1917 to March 1919. In September 1919 25 of the 50 were dead, and in 4 the prognosis was bad, of whom 3 had since died. In 21, or 42 per cent., of the 50 cases the condition was satisfactory in March 1920. In 7 death was directly due to influenza, and in other fatal cases the treatment was not continued or death occurred after considerable improvement (cf. *Medical Science*, 1919–20, **1**, 383). Fernandez recommends small doses of 300-500 c.c. of oxygen repeated at frequent intervals in preference to larger quantities from 1,200 c.c. and upwards, as the small doses avoid causing the patient distress, and are never followed by mediastinal and cardiac displacement.

Eliasberg records the results of six years' pneumothorax treatment at the Berlin University Children's Clinique. She considers that the operation can be performed and kept up in the child just as well as in the adult, and can be well borne even by infants in the first six months of life. the only reaction being a slight increase in the frequency of respiration. At first only children with extensive pulmonary disease were treated, but later an effort was made to attack the disease at its onset. The treatment was at first employed for unilateral disease only, but subsequently cases with disease of both lungs were also treated. The operation was found to have a favourable effect on hilus tuberculosis in the second stage. The fever and cough disappeared, and when a good collapse of the lung was obtained the pulmonary disease did not advance. Cases with haemoptysis did not have a recurrence of their haemorrhage. Lastly, the operation was of value in extensive tuberculosis with cavity formation. The complications observed by Eliasberg were pleural adhesions and effusion and surgical emphysema. No cases of embolism were seen. The intervals between the refills at the beginning of the treatment were three to four days, and when the pneumothorax was complete, they were increased to a fortnight and then to four to six weeks. Two years are regarded as the mininum duration for the pneumothorax treatment.

During the last eight years Schwenkenbecker, of Frankfort, and his assistants have performed artificial pneumothorax in about 100 out of 4,000 cases of pulmonary tuberculosis, or in about 2·5 per cent. In 15 patients who had been kept under observation for a considerable time after the operation, recovery or decided improvement had taken place. In a much larger number aggravation of the condition had occurred, and the treatment had to be discontinued. The relatively largest number of cases consisted of those who for some unknown reason had abandoned the treatment. Schwenkenbecker never recommends artificial pneumothorax if treatment in a sanatorium for the ordinary period promises success, as is the case in the vast majority of patients with tuberculous apical catarrh in the first and second stage of Gerhardt-Turban.

Hoke reports a case of artificial pneumothorax in a girl aged 19, in whom as the result of unusually low intrapleural pressure the manometric fluid, which consisted of a sterilized solution of eosin, was aspirated into the tube and was only saved from entering the pleural cavity by immediate withdrawal of the needle. The case, of which no previous example has been recorded, shows that a sterile antiseptic fluid should always be used for the manometer in artificial pneumothorax.

Borelli, of Turin, emphasizes the importance of oral auscultation, which was introduced by Galvagni in 1875, in determining the condition of artificial pneumothorax. The object of oral auscultation, which is performed by approximating the ear- or the chest-piece of a binaural stethoscope to the patient's mouth, is to detect the sounds produced in the lung while the patient breathes exclusively through the mouth. The value of oral auscultation lies in the fact that râles are sometimes heard by this method when examination of the chest is almost or entirely negative. Most authors are agreed that oral râles are a peculiarity of pulmonary tuberculosis, especially in the stage of cavity formation, and that they are less commonly heard in other diseases of the chest, such as pneumonia, and especially bronchitis. The value of oral auscultation in artificial pneumothorax is due to the fact that the râles may appear or disappear during the treatment according as the pneumothorax is or is not complete, and the lung is in a state of absolute respiratory inactivity or not. On the first signs of resumption of respiratory activity in the lung under treatment an immediate relief is indicated.

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PNEUMONIA

Epidemiology. Epidemics of pneumonia have been recognized for years, but only lately has it been possible to investigate them from the bacteriological point of view. Amongst the blacks in South Africa Lister observed extensive epidemics of a 'typhoid' form (a pneumococcal septicaemia). Stillman was able to prove the wide distribution of the pneumococcus outside the body, and was thus able to place our knowledge of the epidemiology of the disease on a sound basis. In the dust of rooms occupied by patients suffering from pneumonia he isolated the pneumococcus in 74 out of 183 cases and in 30 per cent. the pneumococcus belonged to Types I, II, or III. In the majority of these cases the organism found in the dust of the room corresponded with the type which had caused the disease. In rooms of healthy individuals he isolated in 12 per cent. only those types of pneumococci (I, II, and III), which are not often found in the mouths of persons in good health. It is to be borne in mind that Type IV, although it may cause a pneumonia which has a low percentage mortality, is very commonly found in the throats of people in health. It may be said that the majority of cases of pneumonia are not caused by Type IV, for although this organism was found in 140 out of a total of 297 normal persons examined (Avery), it was the cause of only 92 cases amongst 454 of the disease, the remaining 362 being due to Types I, II, and III. Therefore the cause of pneumonia is more often *exogenous* than *endogenous*.

Nobécourt, Paraf, and Bonnet have carried out extensive investigations at the Maternité upon the question of contagion in pneumonia and incidently have touched upon the question of carriers. For cultures the secretions of the pharynx and also fluid obtained from pleural effusions were used; and to determine the type of organism the method of macroscopic agglutination was employed. Some of their results are quite striking. From March 1 until June 30, 1919, Type I was isolated twice, Type II 16 times, and Type IV 20 times, amongst 38 healthy individuals. Type I was met with in two infants sleeping in a room, where there were carriers of the same organism. Type II was isolated from 9 infants at the breast, whose mothers suffered from sore throats or broncho-pneumonia caused by the same type of pneumococcus. Type II was also found in one breast-fed infant, whose twin brother (fed also by the mother) had an otitis media due to the same organism. Type II was isolated from 5 infants who lay in the same room with carriers of that type. And finally, Type II pneumococcus was recovered from an infant on the first day in hospital.

Amongst 139 persons suffering from nasopharyngitis, tonsillitis, broncho-pneumonia, or empyema, Type I was isolated 10 times, viz. in 5 infants with nasopharyngitis, 4 with broncho-pneumonia, and in 1 woman with tonsillitis. Type II was recovered 117 times, viz. in 35 women with herpetic tonsillitis, 11 women with broncho-pneumonia, in 36 infants suffering from nasopharyngitis, and in 35 babies with broncho-pneumonia, 7 cases of which were complicated by empyema and one case by purulent pericarditis. Type III was found in the pus from otitis media in one infant, and in 2 women suffering from broncho-pneumonia. Type IV (not agglutinating I, II, or III sera) was isolated 3 times, in 3 babies with nasopharyngitis. Finally, in 6 cases the pneumococcus isolated was agglutinated by both antisera I and II, in 3 cases of nasopharyngitis in babies, and in one case of broncho-pneumonia, one of tonsillitis, and one of empyema.

Marked seasonal variations were noted, for in April, May, and June 1919 a pneumococcus was isolated in 79 per cent. of cultures made from the respiratory tract: Type I, 7 times; Types II and III, 3 times each; Type IV in 9 instances. In August, September, and October of the same year Type I was not met with, Type II in 6 cases, Type III in none, and Type IV in 8 cases. From November 1919 until the end of February 1920 the pneumococcus was isolated in 61 per cent. of cases; Type I, 5 times; Type II in 89 cases; Type III in no cases at all; Type IV in 6 cases, and a pneumococcus agglutinable with antisera I and II, 6 times.

One instance of the spread of the infection is worthy of record. In one room there were no cases of the infection but merely one carrier of Type IV. On May 15 a woman was admitted with a herpetic tonsillitis due to pneumococcus Type II. Her child became feverish and developed a nasopharyngitis due to the same type. A short time later a baby placed in a bed exactly opposite had a severe broncho-pneumonia due to the same organism, and another infant, although healthy, became a carrier of Type II, and finally two other babies had nasopharyngitis with fever due to the same type of pneumococcus.

These writers, contemplating the above findings, insist upon isolation of adults, and especially if children are near, to avoid *direct contagion* by droplets of sputum and *indirect contagion* with dust containing pneumococci. They found that curtains of muslin, hung between the beds, did not suffice to achieve this.

Clinical aspects. Nobécourt and Paraf record their investigations, carried out from March 1919 until the spring of 1920, upon pneumococcal infections amongst a large group of *infants* at the breast, ranging in age from a few weeks to four or five months. The exact number of babies examined is not stated. Cultures were made from nasopharyngeal swabs, and it is in this situation that the pneumococcus first lodges. Sometimes it was possible to date exactly the onset of such an infection—when a culture, previously negative, became positive. But some of these infants became carriers only and showed no signs of illness. Generally, however, a coryza appeared, whilst in others the general disturbance was more severe than the local symptoms. In contrast with adults, it is the lymphoid tissue of the nasopharynx rather than the lower pharynx which bears the brunt of the infection. Generally there is fever of 100° to 100·8°, but it may be much higher. As a rule it lasts for only a day or so, but sometimes may continue for ten days or two weeks. With the coryza there is often nasal obstruction and consequent difficulty in taking the breast. There is cough and often diarrhoea and, although other signs are absent, congenital syphilis may be thought of. Then, too, pneumococcal nasopharyngitis in congenital syphilitics lasts longer. The nasopharyngitis may be only the first stage of a mild tracheitis and bronchitis, or may be the precursor (sometimes so mild as almost to escape notice) of a broncho-pneumonia. Almost always the broncho-pneumonia is of the pseudo-lobar confluent variety. In 25 per cent. of the cases there was only a single large patch of frank consolidation, and in 75 per cent. there were two or three patches in one lung or in both. As a rule these areas developed one after the other. When they had once appeared they increased very little in size. Dullness, blowing breathing, and fine crackles were made out. In the pneumococcal cases few large moist râles were present, but these are common if the pneumonia is due to other organisms where there are apt to be many small scattered foci of inflammation. The temperature chart shows many remissions of one or two degrees and defervescence by lysis. True lobar pneumonia in early infancy is rare. About 40 per cent. of the cases died, either from the pneumonia itself or from its complications.

Heiman analyses 336 cases of pneumonia in *infants and children* seen at Mount Sinai Hospital, New York, during the pandemic waves of influenza of 1918 and 1919. Broncho-pneumonia occurred in 288 cases with 51 deaths (17·7 per cent.). Up to the age of 6 months the mortality was 25·6 per cent. and the death-rate varied inversely with age except in those children of 2 to 5 years where it was 15·9 per cent. The lowest death-rate was 9·6 per cent. in children of 5 years. Lobar pneumonia was diagnosed in 41 out of a total of 336 cases, with a mortality of 10·4 per cent. The greatest number of deaths in this variety was found in infants of 6 months to 1 year—33·3 per cent. In agreement with Holt, Heiman notes that the left lower lobe was the one most frequently affected in both forms of pneumonia. In a few cases no physical signs of consolidation could be elicited, but the X-rays showed shadows of infiltration. Heiman found that a leucocyte count below 10,000 with polynuclears below 50 per cent. indicated a very poor resistance. In one case followed by rapid recovery there were 86,000 leucocytes and 95 per cent. polynuclears. The average count was

25,000 with about 80 per cent. of polys. Blood-culture in 10 severe uncomplicated cases were sterile.

Freudenthal has noted *delirium* 14 times amongst 107 children suffering from pneumonia. In one case this appeared at the beginning of the illness and persisted up to the time of the crisis; in others it began just before the crisis and lasted for a little time after it; and finally some of the children were not delirious until after the fall of the temperature—the so-called anaemic delirium or delirium of collapse. This last form did not occur merely in children weakened by severe disease. They were often terrified and thought they were being chased by robbers or animals. Freudenthal does not consider that post-critical delirium is essentially different from that which occurs during the fever, but in the former the child is much more active and restless. The consolidation was apical in 8 of the 14 instances of delirium. Delirium did not come and go with rise and fall of the temperature (Siemerling), but became more marked as a rule towards evening. The prognosis of cases with delirium is, generally speaking, good.

Localized oedema of the chest wall over the site of a pleurisy or empyema has quite often been described, but Ohlmann has noted this sign in 20 infants and children, 15 of whom had pneumonia. The remaining children were suffering from severe illnesses characterized by failing circulation: 3 cases of follicular enteritis, 1 of tuberculosis of the lungs, and 1 with septicaemia arising from infection of the umbilical cord. The oedema was slight and was observed in the region of the nipple, but sometimes extended to the mid-axillary line or across the sternum. It sometimes occurred on both sides simultaneously, and in other cases it was noted first on one side and then on the other. It often disappeared on one side before it had subsided on the other one. If the oedema was bilateral, it did not follow of necessity that the more marked oedema was on the side of the lung more severely affected. The oedema usually showed itself for the first time several days, or even two weeks, after the onset of the pneumonia. It is a sign of a severe infection, for the mortality was 75 per cent. amongst those cases of pneumonia which exhibited it, and amounted to only 11 per cent. in those cases without oedema. Ohlmann regards the oedema as a sign of failing circulation and considers that it appears about the nipples as the subcutaneous tissues are so loose in this region. Some of the cases with oedema about the nipples also showed slight puffiness of the ankles.

Konikow describes a case of influenzal pneumonia in a woman whose *blood-pressure* for two years had never been below 225 and sometimes had been as high as 275. On the third day of disease the blood-pressure was 160 systolic and 100 diastolic. For the next three days it gradually fell until at one time it was 130 systolic and 80 diastolic. At this time lysis began and the blood-pressure gradually rose again, and eighteen days later it had returned to 230 systolic and 100 diastolic: the diastolic pressure increasing more slowly than the systolic. Konikow points out that the fall of blood-pressure was due to weakening of the heart-muscle by toxins, and that he and other physicians during two years had been unable by therapeutic measures to lower it.

Meakins has written a suggestive paper on *shallow breathing* and its bad effects, especially in pneumonia. The shallow breathing does produce anoxaemia (Haldane, Meakins, and Priestley) with periodic breathing, cyanosis, &c., yet with this type of breathing there may still be a large percentage of oxygen in the expired air and in the alveolar air. Meakins shows that the difference in the dissociation curves of oxygen and carbon dioxide helps to explain how anoxaemia may exist although the proportion of oxygen in the mixed alveolar air (made up of air coming from the diseased and also from the healthy lung) may be high. The carbon dioxide tension of the mixed arterial blood may remain at normal level, for the diminished removal of this gas in the poorly ventilated parts may be compensated for by increased removal in the well ventilated areas. For oxygen pressures above 88 mm. of mercury little more oxygen is taken up by the blood. 'Thus it follows that in the well ventilated parts of the lung first the increased ventilation is incapable of yielding an excess of oxygen to the blood sufficient to compensate for the lack of oxygen in the blood from the badly ventilated parts, and second, since more than the average amount of fresh air is passing through these alveoli, while no more than the normal amount of oxygen is being absorbed by the blood, the air expired from these well ventilated alveoli must be abnormally rich in oxygen.'

Anoxaemia itself causes shallow breathing, and it is possible that a vicious circle may be established. Prognosis in pneumonia does not necessarily depend on the extent of lung involvement, but from the rate of the respirations we can judge the severity of the disease. As Meakins points out, if this rate in an adult goes up above 50 per minute then cyanosis (a sign of anoxaemia) develops. Cardio-vascular collapse is a result of anoxaemia, but it has not been proved that failure of the heart is the cause of cyanosis. With gradual heart failure blood-pressure falls and a condition of grey cyanosis shows itself. Meakins has studied the amount and quality of expired air of pneumonic patients and gives a table which is full of interest. As the respiratory rate quickens the volume per respiration decreases, but there is a marked increase in the total ventilation per minute; there is a marked diminution in the ratio between the volume of each respiration and the theoretical 'dead space', so that the air expired and inspired may finally amount to but a few cubic centimetres and great cyanosis occurs. The respiratory quotient may even be as high as 1·2. With the crisis the whole picture changes, although there is no rapid increase in the amount of functioning lung tissue; the respiratory quotient becomes normal, and the respiratory rate, volume, and total ventilation rapidly return to that of health. It has been a moot question whether the pulmonary circulation is interfered with or not in pneumonia, and Hoover says that it usually is not. He considers that the cyanosis is due to the non-aerated blood from the consolidated lung entering the systemic circulation. Hoover also claims that cyanosis persists after the crisis until the exudate in the lung is absorbed. Meakins, on the other hand, considers that the X-ray pictures of Gross (taken of injected lungs in fatal cases) prove that the vessels are compressed and that circulation is impeded, but that this phenomenon alone is not important enough to account for the cyanosis. If the flow is obstructed it seems difficult to reconcile this with the following statement: 'in the badly ventilated parts of the lung the volume of blood flowing per minute will be greater in relation to the amount of fresh air entering these parts than in the well ventilated regions' (Haldane, Meakins, and Priestley). No explanation is offered by Meakins as to the cause of shallow breathing in the first place.

The *crisis* in pneumonia remains to-day one of the most interesting phenomena of immunology and clinical medicine. Thomas and Parker give the results of lung puncture in lobar pneumonia and show the significance of this in an attempt to explain the nature of the process which leads to recovery. Such punctures have already been done by a number of workers; Rosenow did 48 in 27 cases, 26 of which gave positive cultures, and the remaining 22 were sterile. Positive lung punctures were obtained at all stages of the disease, but the percentage of these was much higher in the early stages of favourable cases, whilst in fatal cases they were more common in the later stages of the disease than in those patients who recovered. Thomas and Parker punctured the lung 73 times with positive results in 42 and negative in 31. Comprehensive tables are given of the results on different days of disease with the types of organism found. Also the types of pneumococci isolated from the sputum in these patients with negative lung puncture are added. Only two of the patients died, in whom lung puncture was negative. One died 5 days and the other 3 days after puncture. These workers agree that a satisfactory explanation of this phenomenon is not to hand, unless one assumes the possibility of a local recovery in the lung. In some cases at autopsy, where there had been extension from one lobe to another, a stage of resolution may be found in the lobe first affected, whilst in another, grey, or even red, hepatization may be seen. The two fatal cases, mentioned above, had such an extension to another lobe.

Positive results were obtained on every day of the disease, even on the day of crisis, and twice after the temperature had become normal. But, with Rosenow, Thomas and Parker have found that in those cases which ultimately recover the organisms may diminish to a great extent before the crisis, for in the non-fatal cases one negative puncture was obtained four days before the crisis, two on the third day before it, and in six cases two days previous to the critical fall of the temperature. It would, therefore, not seem to be true that there is a sudden destruction of the pneumococci at the time of the crisis, for, were this the case, one would expect to obtain positive lung punctures quite regularly right up to the time of crisis and none at all after this had occurred. In the opinion of Thomas and Parker 'the organisms may be killed twenty-four or more hours before crisis, or may continue to exist twenty-four hours after crisis. Thus the two mechanisms, i. e. bactericidal and detoxifying, are somewhat independent of one another, the second taking place at a given time after the first has gained control of the infection and a pseudo-crisis may even occur before the infection is properly under control.' As these writers point out, the idea of two mechanisms, the bactericidal and detoxifying, is not a new one, but their results seem to lend it additional support.

The recent work of Bull appears to show that antiserum is active on account of its agglutinating and bacteriotropic properties, and that whole blood of passively immunized animals brings about opsonization of the pneumococci, and these organisms are phagocytized by the polynuclear leucocytes, but a pneumotoxin or antitoxin has not been demonstrated. As Thomas and Parker show, the existence of a toxin seems possible, for by assuming its presence we can explain necroses in the liver, suprarenals, pancreas, and kidney. These changes are seen after death although no organisms can be demonstrated in these organs. Such lesion can be caused by injecting a bacterial exotoxin. But we do not know if an anaphylotoxin preformed in the pneumococcus, which is 'haemolytic and mildly antigenic' (Cole and others), can bring about the same changes. All this does not explain the phenomenon of the crisis. Thomas and Parker point out that the recent biochemical work of Jobling, Petersen and Eggstein, and of others, strengthens the possibility that the toxaemia in pneumonia is due to the constituents of the exudate in the lung and that the detoxication is due to an increase or alteration in ferment action, by which the toxic products are rendered non-toxic.

The writers conclude that (1) the death of the pneumococcus is not the factor which causes or initiates the crisis, and (2) the bactericidal and detoxifying mechanisms act, in a measure, independently.

Complications. Nobécourt and Paraf found that *otitis media* was a very frequent complication in nasopharyngitis and broncho-pneumonia in infants. As the drum becomes perforated so easily, and as the condition does not appear to be so painful in the very young, it may pass unnoticed. It is often bilateral. Prognosis is good, mastoiditis does not often occur, the writers saw no meningeal complications, and as a rule the discharge ceases in 10 days or two weeks and a cure is effected. *Empyema* was diagnosed by needle puncture in one case out of every seven of broncho-pneumonia. Often the exudate was haemorrhagic. As the lung puncture was done as a routine to obtain cultures it could be stated with certainty that the majority of empyemas appeared during the course of the pneumonia, but sometimes followed it. One case of a baby with broncho-pneumonia showed a purulent pleurisy on the ninth day due to Type II pneumococcus. This apparently was cured by tapping and the temperature dropped, but rose again, and signs of broncho-pneumonia were again found and, although no fluid could be withdrawn from the pleural cavity, the child died of pneumonia on the twenty-first day. Only two of the cases of Nobécourt and Paraf had *pericarditis*, but an autopsy was done on only one of these. They emphasize the difficulty of diagnosing this complication in infants. Signs attributable to a pneumococcal septicaemia were rare, but two babies had *purpura*. Two had pneumococcal *meningitis* and rapidly succumbed; one of these showed purpura. No cases of arthritis or peritonitis were observed.

Heiman saw 75 cases (40 bilateral) of acute *otitis media* amongst 336 cases of pneumonia in influenza in infants and children. *Empyema* was found 17 times, and treatment by aspiration, until the pneumonia is over, is recommended. *Meningism* occurred in 8 cases, and, if very severe, cerebrospinal fluid was withdrawn to relieve pressure. Pneumococcal *meningitis* (Type I) developed in one case and proved fatal. *Lethargic encephalitis* complicated 3 cases. In one child *hemiplegia* occurred and also an embolus lodged in the right external iliac artery, and the lower limb had to be amputated. Twice there was *spontaneous pneumothorax* and once diffuse *subcutaneous emphysema*. Purulent pneumococcal *pericarditis* developed in one case in which Type I pneumococcus was grown from the blood. An operation was done, but the child died of continued general infection.

During the epidemic of influenzal pneumonia several cases of haemorrhages into the sheath of the rectus abdominis, following rupture of that muscle, were described. In some of these the streptococcus was found. Kummer reports a case of a large *abscess in the space of Retzius* (behind the recti) in a girl of 18, following pneumonia of influenza. This was opened and more than a litre of coffee-coloured pus escaped. Cultures showed pneumococci alone. The wound healed without delay.

Kummer describes a case of slowly resolving pneumonia in a man of 55, following which oedema appeared in both arms and the patient suffered from great dyspnoea and dysphagia. After a few days swallowing became impossible. A large swelling appeared at the site of the lower part of the left lobe of the thyroid. This increased in size until the neck measured 44 cm. in circumference. There were no signs of pressure on the recurrent laryngeal nerve or sympathetic. The swelling was cut down upon and a cyst the size of a small gourd was found in the thyroid, extending down behind the sternum and pressing on the superior vena cava and the aorta. In trying to enucleate it the cyst burst and a large amount of greenish pus escaped. After drainage the wound healed well and the patient recovered completely. Cultures gave a pure growth of pneumococcus. Microscopically it was seen that there had been a very small haemorrhage in the thyroid, and here, in a place of lowered resistance, the pneumococcus had gained a foothold and had produced the large abscess. Kummer refers to the literature of *acute thyroiditis due to the pneumococcus* and records 13 examples.

Haemorrhage into the stomach in lobar pneumonia is very rare. The case of a female aged 50 is reported by von Friedrich. There was no history of any previous trouble with her stomach. She was admitted nine days after a typical onset of lobar pneumonia with signs of consolidation of the right lower lobe. On the thirteenth day there was slight jaundice, and on the fourteenth she collapsed suddenly and vomited a little blood; two hours later she passed much fresh blood in the stool and shortly afterwards died. At autopsy there was pneumonia as diagnosed, but no peritonitis, although the intestines were filled with black semi-fluid matter. The intestinal mucosa showed no lesions. The stomach contained a large mass of blood-clot weighing 620 grm. The gastric mucosa was pale, with here and there haemorrhagic points, where the blood could not be washed off. About the middle of the greater curvature was seen a defect in the mucous membrane the size of a half-pfennig piece, in the centre of which lay the mouth of a small blood-vessel; other smaller areas denuded of mucous membrane were also seen, but these showed no blood-vessel. Serial sections were made, but merely the usual picture of 'haemorrhagic erosion' of the stomach was seen: necrosis of the mucous membrane, congestion of the surrounding blood-vessels, and small round cell infiltration. No micro-organisms were detected and there was no thrombosis. The case occurred during the time of an epidemic of influenza (March 1920) but von Friedrich, perhaps unjustifiably, considers that the patient had suffered from acute lobar pneumonia. It is assumed that the toxins of the pneumococcus cause an injury to the small blood-vessels in the stomach wall. Dieulafoy has described cases of pneumonia with haemorrhage into the stomach, and in one of these the capillaries of the mucosa were filled with pneumococci. The difficulty of diagnosis between haemorrhage from 'erosion' and haemorrhage from gastric ulcer is emphasized by von Friedrich, and, little as we know of the causation of the latter lesion, the nature of the former remains still more obscure.

Pneumonia with co-existing multiple arthritis. Greenberg reports an interesting case of lobar pneumonia in a man; on the second day of disease frank signs were present over the left lower lobe and the predominating organism in the sputum was a pneumococcus of Type IV. On the third day his condition was much more serious, he was very cyanosed, and the consolidation had spread to the left upper lobe with an additional patch in the right lower one. That evening he complained of great pain in the left shoulder, which was thought to be due to the extensive pleurisy on that side. The following day he had arthritis in the left knee and right ankle, which were red, swollen, and tender. His temperature came down by rapid lysis. The picture became that of acute rheumatism with shifting pains and involvement of both knees; in the course of a week both ankles, both elbows, and left hip were affected. Pneumococcal arthritis was suspected when the first joint was involved, but there was no septic temperature, the patient responded readily to salicylates, and there were small erythematous patches about the joints, so the suspicion was not well founded. Eventually recovery was complete, but for nine or ten days after the early fall of temperature there were still signs of consolidation in the lungs, and even after three weeks signs persisted at the left base. Greenberg points out that it is interesting to note that the temperature fell almost simultaneously with the onset of the acute articular rheumatism, and draws a parallel between the effect of this added new type of infection upon the lobar pneumonia and the good results sometimes obtained in treating infections with non-specific vaccines. It is well known that *in vitro* some micro-organisms have a favourable and some an inhibitory effect upon the growth of others. May this also not obtain *in vivo*?

Treatment. Nobécourt and Paraf strongly advise *isolation* to prevent spread of pneumococcal infections amongst infants.

These authors employed antipneumococcal sera (I or II), prepared at the Pasteur Institute, by injecting them into the hepatized lungs of the infants under their care. Five to 10 c.c. were used and there were no ill effects beyond an attack of coughing. If there is more than one focus of pneumonia each must be treated in the same way. In case of a purulent pleurisy the fluid is withdrawn and replaced by serum of the appropriate type. Twenty-one cases of broncho-pneumonia, 15 of which were severe, were treated in this way. Four patients with a rapid onset, and only one area of consolidation, but severely ill, were given 2 to 4 injections and all recovered. Six others with a more gradual onset, but in which there were several areas of pneumonia, received injections at a later period (4th to 7th day); 3 of these recovered and 3 died. In the remaining 5 cases, broncho-pneumonia followed nasopharyngitis. Two of these recovered and 3 died, one of broncho-pneumonia which came on after varicella, another had extensive streptococcic dermatitis, and the third died of pneumococcal meningitis. Therefore 9 recovered of the 15 treated. Six babies with purulent pleurisy were treated by replacing the fluid with antiserum, and 4 recovered rapidly, one (mentioned above), although cured of the purulent pleurisy, died of streptococcic dermatitis, and the other of pericarditis. Nobécourt and Paraf rely wholly on the local effects in the lungs of the serum in these cases. Of 4 others treated by intramuscular injection of antiserum, 2 recovered and 2 died.

Gray records his results in the treatment of pneumonia with *Kyes's antipneumococcus serum*, which is prepared by injecting an insusceptible host ('the ordinary barnyard fowl') with a large number of living pneumococci (vide *J. Am. M. Ass.*, 1911, **56**, 1871–81). The antiserum so produced is said to be very rich in antibodies. Cases were treated at the Base Hospital, Camp Grant, Illinois, by administering the serum intravenously in doses of from 5 to 10 c.c. twice daily, a total of 60 to 90 c.c. generally being given. Gray states that the so-called 'foreign protein' reaction was noted in only about 5 per cent. of the cases, so that this non-specific reaction cannot be considered as an important factor in reducing the mortality. Except that the serum is antibacterial nothing more definite may be said of its action. Kyes considers that the treatment is still in the experimental stage and the serum has not been prepared for general use. All the cases of pneumonia could not be treated with it as a sufficient quantity was not available. The results are quite striking when one considers that, with the exception of the use of antiserum, all the patients had the same general treatment. Between September 21 and November 4, 1918, 234 cases of 'epidemic pneumococcal broncho-pneumonia' received antiserum and the death-rate was 16·7 per cent., as compared with a mortality of 53·6 per cent. in the 1,684 control cases. Between November 5, 1918, and May 1, 1919, 118 cases were treated with serum, and in these there was a mortality of only 4·3 per cent. During this latter period the cases were of an atypical pneumococcal pneumonia, 'which seemed to indicate a gradual change from the epidemic type back to the type of lobar pneumonia, probably due to a falling virulence of the organism'. Also 11 cases of pneumococcal meningitis were treated with the antiserum (intrathecally and intravenously) and 5 recovered.

Monguzzi, in a very just article, gives a *résumé* of the various views held regarding the nature of effects produced by *foreign protein therapy* and also adds an account of 22 cases of lobar pneumonia or broncho-pneumonia treated by this method in the autumn of 1919 and winter of 1920. Monguzzi does not consider any cases admitted later than the third day of disease.

The first group of 11 cases received on the day after admission a single intramuscular dose of 10 c.c. of milk sterilized by boiling. The results were surprisingly favourable in all of these, for within 36 hours of the injection resolution had set in and apparently the attack was aborted. The thermal reaction which followed the injection was quite marked in all and violent in some. There was a slight chill in two cases only. The fever was markedly decreased within six to nine hours and the patients felt better. In 2 cases the temperature was normal by the fourth day; in 7 by the fifth day; and in 2 on the sixth day. The local reaction was sharp and painful, but the inflammation subsided in the course of a few days.

In the 7 cases that make up his second group a similar intramuscular injection of milk was given the morning after admission, but was followed by such a slight elevation of temperature, as compared with the degree of fever present the previous evening, that it was uncertain if the rise could be attributed to the injection. A second injection of milk was given 24 hours after the former one, with another feeble thermal reaction, but the patients felt better, the amount of urine increased, and the temperature and pulse-rate fell gradually. Forty-eight hours after the second, a third dose was administered, which was again followed by a slight reaction. The temperature, however, came down by lysis, and reached normal by the 7th to 9th day, and *redux crepitus* was heard over the resolving lung. Recovery was rapid after this.

The third group treated consist of 3 cases admitted on the 2nd or 3rd day of disease. Milk (10 c.c.) was injected on the 1st or 3rd day after admission, but the temperature did not rise more than 0·5° C. and was not followed by any objective or subjective improvement. It is noteworthy that in these three cases, although the patients were seriously ill, the fever was not high. Monguzzi, on the 4th day after admission, then gave each patient an intramuscular injection of two thousand million of a stock gonococcus vaccine as another form of foreign protein. A slight chill but sharp thermal reaction followed. There was subjective improvement and signs suggestive of beginning resolution were made out. A similar dose of vaccine was given the next day with a sharp thermal reaction as a consequence and from that time on recovery was rapid.

One patient who was extremely cyanosed and gravely ill makes up the fourth group. One injection of milk, followed the next day by an injection of stock gonococcus vaccine, failed to produce much reaction or general improvement. He died on the sixth day of disease.

Two distinct results were noted after the use of foreign protein: (1) an immediate general improvement following the thermal reaction, and (2) a less rapid effect indicating beginning resolution in the lung with *redux crepitus* and increase of sputum. Absence of marked thermal reaction does not suggest a favourable prognosis. Monguzzi does not think that sterilized milk injections form the method of choice, but favours the giving of foreign protein in stock vaccines. He is moderate in his claims for the treatment in his small series of cases.

Heiman discourages the use of *digitalis* in children with pneumonia, stating that the blood-pressure is not increased by the drug and the heart-rate is not lowered. ‘As auricular fibrillation is a very rare complication in the pneumonias of children, its use to prevent this condition is but an ephemeral theory.’

Much has been claimed for *camphor* in the treatment of pneumonia: (1) it is stimulating to the heart-muscle and raises the blood-pressure by acting on the vasoconstrictor centres; (2) the pneumonic exudate is more quickly absorbed as the pulmonary vessels are dilated, and thus more blood with more polymorphs and their ferments are determined to the lungs; (3) it is said to exert a definite bactericidal action on pneumococci; (4) it brings comfort to the patient as it lessens pain; (5) the temperature falls earlier and usually by lysis; and (6) the mortality is lowered by its use. Klein summarizes the present views on camphor and also points out the dangers in its use. A patient of his, a student of 19, suffering from a relatively mild attack of broncho-pneumonia without severe circulatory disturbance, received two doses a day on the 3rd and 4th days of disease (10 c.c. of ‘Ol. camph. forte’). About half an hour after the 4th and last dose he complained of general discomfort, quickly became deeply cyanosed, lost consciousness, the radial pulse could not be felt, and finally respiration ceased entirely. By means of artificial respiration kept up for forty minutes, intravenous injections of caffein, digalen, and adrenalin, the patient finally came round. The next day, without a further dose of camphor, he had another attack, lost consciousness, and his respirations ceased though his pulse remained quite good. Recovery followed the same treatment as on the former occasion. From that time forth his progress was favourable and his temperature became normal on the 8th day. Klein suggests that instead of causing delirium, hallucinations, &c., as camphor may do, there was paralysis of the respiratory centre in this case. The camphor oil was analysed, was found to be pure, and contained no oxycamphor, which is known to paralyse the respiratory centre.

Siciliano sounds a note of warning against the acceptance of all that has been claimed for the treatment of pneumonias by means of sodium citrate (vide *Medical Science*, 1920, **2**, 514), especially as we do not fully understand the vagaries of the disease in influenza, and as sometimes the general condition of the patient may rapidly improve without special treatment. Many patients, during the epidemic of influenza, had sharp attacks of epistaxis and others of haemoptysis, so that it does not seem wise to lessen the coagulability of the blood in all cases by giving sodium citrate. Siciliano records the case of a young man with influenza, an initial symptom of which was epistaxis. Following immediately upon a dose of 5 grm. of sodium citrate in the course of twenty-four hours, epistaxis occurred again and with this haemoptysis.

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A. M.

AIR EMBOLISM FOLLOWING THORACOCENTESIS

Air entering a pulmonary vein and causing air embolism following puncture of the lung. When death has followed upon, and has appeared to be due to, puncture of the chest, it has been attributed to a nervous reflex from the pleura acting upon the heart and respiration by way of the phrenic and pneumogastric nerves. As the accident has been only exceptional in its occurrence, it has been necessary to assume that the patients so affected have had especially excitable nerves. One reason for this conclusion has been the absence of anything found *post mortem* to account otherwise for the occurrence. On this view the death has been regarded as both unforeseen and unpreventable.

But a consideration of a number of cases has shown that an immediate cerebral disturbance has been set up, giving rise to signs both of paralysis and excitation. This can be traced to an entrance of air into a vein of the lung, the air passing in particular to disturb the circulation through the cerebral arteries, although at the same time there may be air emboli in the coronary arteries, also in superficial blood-vessels causing disturbance of the circulation in general and in the skin.

In addition to the occasional supervening of this accident when exploring the chest with a hollow needle, or when washing out an empyema cavity, there have happened a number of cases since the introduction of the treatment of pulmonary tuberculosis by instituting an artificial pneumothorax. By taking special precautions, the entry of air into a pulmonary vein may be prevented.

A fact which tells against the theory of a pleural reflex is that after an empyema cavity has been irrigated many times, and after air has been often let into a pleural cavity, on a repetition of the procedure, sudden grave symptoms have arisen. Cases will be mentioned in which such symptoms failed to give warning of danger, and the next pleural irrigation or introduction of air proved fatal.

Raynaud, in 1875, in describing cases of death occurring during and after thoracocentesis, confused together different conditions. One patient died suddenly as the skin of the chest wall was being cut by a lancet, preliminary to plunging a trocar into an empyema, others died suddenly as the trocar entered the empyema, or whilst the pus was escaping. Terrillon, in 1873, had collected 30 cases in which the tapping of an hydatid cyst of the lung caused the lung to be suddenly flooded with the fluid from the cyst under high tension. But there were other cases in which quite different results followed, and which were evidently signs of cerebral paralysis and excitation. In one case mentioned by Raynaud an empyema cavity had been irrigated regularly for two months, when on repeating the irrigation the patient suddenly turned deadly pale, became unconscious, and the pulse and respiration failed. There followed convulsions, involving all four limbs and the face, blood-stained foaming at the mouth, and involuntary evacuations. After a period of stertor and coma, he gradually became conscious, paresis of the right arm persisted for ten days, and then all this disturbance disappeared. In another case an empyema cavity was being irrigated, as had been done many times before, when suddenly there was extreme pallor, trembling of the lips, convulsive movements of the arms, and half an hour later the patient complained that he could not see. There was found ischaemia of the optic disks with congestion of the surrounding retinal vessels. After an interval the irrigation was repeated, when there was a sudden collapse into unconsciousness. Clonic convulsions of the limbs set in with conjugate deviation of the head and eyes, the pulse-rate rose to 150, and coma, alternating with convulsions, continued until death during the night. Raynaud attributed the death to reflex action through the phrenic nerve.

Vallin had irrigated an empyema cavity for six days without incident, when, whilst doing so, there was sudden unconsciousness, opisthotonos, dyspnoea, a pulse-rate of 140, and death followed on the 7th day without there being any return of consciousness. Vallin called the convulsion eclamptic. At the same time a case under Brouardel was reported in which an empyema cavity had been irrigated for twenty days with spirit lotion, when, on repeating this, there was sudden clenching of the teeth, foaming at the mouth, clonic movements, especially of the left arm, followed by deep sleep for an hour. Next day, the patient had no memory of the accident. Three days later the cavity was again irrigated with the same lotion, when more severe symptoms of the same kind at once supervened with involuntary evacuations followed by death. Cayley, in 1876, after describing his case, remained undecided whether to attribute death to cerebral embolism or to reflex action. An empyema cavity had been irrigated many times when on its repetition there was suddenly a deadly pallor, a very slow pulse, deep unconsciousness, and the pupils widely dilated; then the face flushed, and the breathing and pulse became extremely rapid. There followed irregular convulsions of all the limbs, turning of the head and eyes to one side, involuntary evacuations, the temperature rose to 107° F., the pulse-rate to 142, the respirations to 72 before death in general convulsions.

Goodhart's case was a girl of 16, in whom a right-sided empyema of some two months' standing was tapped by a large trocar and cannula, a drainage-tube being inserted through the cannula. She had been subsequently irrigated twice daily for about five weeks, when, whilst sitting up during the irrigation, she suddenly turned livid and fell back unconscious. She ceased to breathe, and no pulse could be felt at the wrist. After artificial respiration for ten minutes the breathing and pulse returned, but she remained completely unconscious. The colour returned to her face, but an hour later her right face, arm, and hand appeared blue and congested. Urine and faeces were discharged involuntarily. Later, the colour of the head and neck became symmetrical, and there was profuse sweating. The legs were not affected. The respiration rose to 40, the pulse-rate to 120, whilst the temperature took the reverse direction to Cayley's case and had fallen to 94·4° F. before death. The pupils, at first contracted, were later dilated. A transitory paralysis of the right face, alternate movements of the arms, opening and shutting of the eyelids, movements of the eyeballs, semiconvulsive respiratory movements, slight convulsive movements of the mouth, were noted whilst the patient was deeply unconscious. Beyond the right-sided empyema, which was nearly obliterated by adhesions, and the collapsed lung, a complete post-mortem examination discovered nothing, no clotting either in the cerebral or coronary arteries.

Goodhart appears to have considered that the clinical signs pointed to embolism, but there was an absence of post-mortem lesions to confirm this view.

Jeanselme, in 1892, made a collection of 45 cases of what he called nervous accidents following thoracocentesis and the irrigation of empyemata.

Stephen Paget, in 1896, and again in 1902, concluded that these accidents when washing out the empyema cavity were all due to reflex action. Although he described the convulsions as epileptiform, he said that they were not due to true epilepsy.

A. E. Russell, in 1901, fixed on a reflex effect through the vagus upon the heart, the cerebral symptoms being due to the anaemia consequent on the cardiac inhibition. Wilson Fox had collected 32 cases following puncture of the chest, of which 20 were attributed to syncope and 6 to asphyxia. 17 cases which died within 48 hours of the puncture had their death, at any rate accelerated, if not immediately caused, 7 by syncope, 5 by asphyxia, in 3 of which there were signs of pulmonary oedema, and 1 by haemorrhage. In the remaining 4 convulsions had preceded death. In 3 cases noted by Russell the needle entered the lung.

Case I. A girl of 8, with pneumococcal pneumonia, immediately on puncture at the left base became unconscious; there was a small amount of frothy blood in the mouth and nose, the colour became livid, there was a strong double convergent squint, and some rigidity of the arms. The pulse could not be felt, the heart-sounds were inaudible, the breathing slow and gasping for a minute and then it ceased. There was no response to artificial respiration, saline infusion, or stimulating injections. The left pleural sac had been obliterated by adhesions of long standing; the left lung presented multiple bronchiectasis and suppuration.

Case II. A girl of 7 was explored with a needle at the right base, some blood returned through the needle, there was at once pallor of the right side of the face with other patches of cyanosis and unconsciousness. There continued convulsions alternating with coma, involuntary evacuations, and a weak pulse until death five days later. There was no empyema or pleural adhesions; the base of the right lung was collapsed; the vessels of the pia mater were injected with scattered haemorrhages.

Case III. A man of 54 had old-standing pulmonary tuberculosis. On the first puncture of his left base, he felt no disturbance; as nothing escaped by the needle, a second puncture was made close by, when a little blood returned through the needle. Immediately he evacuated a large quantity of urine, turned pale, and fell back unconscious. He stopped breathing, and artificial respiration had to be adopted for half an hour. He then had alternating convulsions and hemiplegia on the left side with irregular rigidity. Involuntary evacuation and irregular convulsions continued until death three days later. There was nothing found except the old-standing pulmonary tuberculosis. Russell said that this last case was suggestive of cerebral embolism, but there was an absence of any lesions *post mortem* in confirmation.

Forlanini, of Pavia, commenced his treatment of pulmonary tuberculosis by an artificial pneumothorax in 1882; referring in 1904 to accidents which had occurred, he used the term eclampsia. Sundberg, in 1913, recorded three fatal cases which had happened.

Case I. A fairly strong woman of 28, with pulmonary tuberculosis, had had gas introduced into the pleura seven times; at the eighth time, on being punctured with the hollow needle, and before any gas was turned on, she suddenly became deadly pale, lost her voice, threw her arms about, opened and shut her mouth, ground her teeth, and then became unconscious with a quick pulse. She remained unconscious, making irregular movements and involuntary evacuations until her death 36 hours after. No puncture of the lung was discovered; there was venous congestion of the cerebral cortex, but no gas bubbles in the cerebral arteries.

Case II. A man aged 49, with pulmonary tuberculosis, was punctured three times without the needle entering the pleural cavity, and so no gas was let in; then for eighteen times the needle entered the cavity, and so gas was introduced. Having been punctured for the twenty-second time and 300 c.cm. of gas having passed in, the needle had been withdrawn and the puncture closed, when, two or three minutes later, the patient was seized with inspiratory dyspnoea whilst retaining his voice; he became deadly pale and broke out into a sweat, felt as if he could not fetch his breath, then became comatose and died three hours afterwards. The lung was found so collapsed as to have rendered puncture out of the question; it was deemed impossible for the gas to have been injected into the lung, and no gas was noted in the blood-vessels.

Case III. A young man with pulmonary tuberculosis, in whom a previous introduction of gas had caused temporary dyspnoea. A second, three days after the first, commenced with salt solution, then with nitrogen gas, and there was no disturbance until the sixth introduction, when there was sudden pallor and cyanosis in patches, unconsciousness, foaming at the mouth, convulsions, and death in about a quarter of an hour. In this case a puncture was found in the lung, and there were gas emboli in the vessels of the cerebral cortex.

In 1912 Brauer directed attention to the question of air embolism of the cerebral vessels. Wever had found by experiments on monkeys and dogs that similar effects could be produced by the introduction of as little as 0·2 c.cm. of air into the common carotid artery. He, with Spengler, described four cases of such accidents when setting up a pneumothorax.

Case I. A woman of 24 had had gas let into the pleura on two occasions. On the third the needle penetrated the lung when the patient at once collapsed; she frothed at the mouth, and the breathing and heart-sounds ceased. Only after an hour of artificial respiration did she breathe again, and the heart-sounds could be heard. There followed clonic convulsions, alternating with hemiparesis on the right side, including the face. The next day there were some signs of recovery followed by relapse and death.

Case II. In this case also the needle penetrated the lung and there followed collapse and death. The patient had had gas introduced into the pleura once before without disturbance.

Case III. A woman had had pulmonary tuberculosis for six years when a pneumothorax, it was supposed, was established. Five days later, when gas was again introduced into the pleura, she suddenly died. It was found that the lung was completely adherent to the chest wall, the needle had punctured a large vein in the lung into which the gas had entered.

Case IV. A girl of 18, with left pulmonary tuberculosis, had had 100 c.cm. of nitrogen gas introduced when she suddenly became unconscious with convulsions and died in six hours. The gas had entered the lung, and there were gas bubbles in the capillaries of the brain.

Schlaepfer quoted the case by Saugman of a woman, aged 32, who had been long ill with pulmonary tuberculosis. The needle connected with a manometer was inserted for 3·5 cm. when the manometer showed only small excursions, so a stylet was passed, and on drawing this out a little blood followed. At that moment the patient said she felt giddy, and the needle was at once withdrawn. She turned pale, and was laid on her back; she was unconscious, the head and eyes turned to the left with contracted pupils. Then the respiration became irregular and failed, the pupils dilated, and she died. The needle had penetrated a vein in the lung, and there were found gas bubbles in the blood-vessels at the base of the brain, including the sylvian artery.

With the entry of air through the wall of an empyema may be compared Brandes's case, in which death followed the injection of bismuth paste into an empyema sinus. A man of 30 had had a persistent sinus for ten months, when 10 c.cm. of bismuth paste was injected without disturbance. Three days later 40 c.cm. of the paste was inserted through a rubber catheter under very little pressure, most of the paste escaping at once beside the catheter. The patient became suddenly unconscious with stertorous breathing, deviation of the eyes to the right, and intermittent general spasms. Coma persisted, and after Cheyne-Stokes breathing, he died in twenty hours. The bismuth was found in the smallest blood-vessels of the cerebral cortex, especially of the left hemisphere, but also on the right side. On examination under the microscope of the wall of the empyema fistula, the entry of the bismuth paste was traced into pulmonary capillaries, where the catheter had detached granulations lining the cavity and had opened up venules. There were traces of the bismuth paste in other capillaries of the general circulation besides those of the brain.

In Jessen's patient it was intended to inject the wall of the thorax with a local anaesthetic before proceeding to explore for a pulmonary abscess. The needle, entered from behind, penetrated the lung; the patient began to cough, suddenly became unconscious, with partial pallor and cyanosis of the face, twitchings of the arm, and blood-stained sputa. Deep unconsciousness continued until death sixteen hours later. The lung had been punctured, but no gas bubbles were found in the vessels on the surface of the brain.

Schlaepfer's review of the subject was started by a case under Clairmont at Zürich. A railway guard, aged 34, had suffered from a recurrence of bronchitis which developed into broncho-pneumonia. On the supposition that an abscess had formed, the right lung was punctured in two places without result; six days later the puncture was repeated in several places, equally without result. After a further period of nine days, the back of the right lung was exposed by removing a segment of the 4th rib under local anaesthesia. The lung was punctured, and some bloody fluid withdrawn by a syringe; the syringe being detached for examination of the fluid, the hollow needle remained in the lung. At once the patient collapsed and became unconscious, with the pupils fixed midway, and clonic twitchings all over the body. The unconsciousness lasted some minutes; the patient recovered in about 2½ hours, when he complained that he could not see and for three days was quite blind, but ophthalmoscopic examinations did not discover anything abnormal. For a fortnight he could not read for giddiness, and it was only after six months that his vision became as good as before. Some days after the exploration of the lung, there was an increased mucopurulent expectoration, following which the pulmonary signs subsided; the exploration wound healed in three months, and the man was able to return to his occupation.

The instances given above, with many others to which Schlaepfer refers in his review of the literature, afford clinical evidence of the results of air embolism involving especially the cerebral vessels, also coronary and cutaneous arteries. The signs of this air embolism vary in degree, but are all sudden in onset. There is pallor of the skin alternating with patches of cyanosis, so that the skin may have a marble-like appearance. The patient complains of feeling giddy or ill, has pain in the chest or head, and may cry out; black patches appear before the eyes, or he says that he cannot see at all. Often suddenly, sometimes after a short delay, there is an entire loss of consciousness. The pulse is suddenly altered: it may be at first very slow, afterwards rapid, or immediately very weak. There is dyspnoea passing on to stertor and periodic breathing, or at once the breathing may be rendered superficial and gasping. The pupils in the slighter cases contract and become unequal; in the dangerous cases they dilate at once and there is a loss of the corneal reflex. There is plain evidence of the excitation of the sensorimotor areas of the cerebral cortex in the conjugate turning of the head and eyes, nystagmus, and squinting. There set in irregular tonic and clonic convulsions affecting the muscles of the limbs, alternating with paresis. A spasm of the back muscles may produce opisthotonos and involuntary evacuations occur. The patient remains comatose until death after a varying period of hours or days.

When consciousness is retained or recovered there may still be signs referable to the cerebral cortex, disturbances of sensation, hyperaesthesia, anaesthesia, ant creepings, also impairment or loss of speech.

The slighter cases recover within ten days, except so far as regards vision.

The difficulty in recognizing air embolism as the cause appears to lie in the slight character of the changes found *post mortem* in the brain.

In the cases where there has been bronchiectasis and pulmonary abscess, septic softening of the cortex cerebri, including gas bubbles in the capillaries, may be put down to septic decomposition. But gas bubbles have been noted in some cases in the capillaries of the pia mater, also congestion, haemorrhages, and commencing softening, which could not be attributed to septic decomposition. There have been already quoted experiments by Wever, who found that cerebral air embolism could be produced in monkeys, also in dogs, by injecting into the carotid artery as little as 0·2 c.cm. of air.

The prevention of such accidents:

(1) In puncturing the chest by means of a hollow needle with a syringe attached, if the syringe is detached, a deep inspiration on the part of the patient may draw air in. If simply a hollow needle with a stylet is used, then air may be sucked in when the stylet is withdrawn. The accident does not happen unless the point of the needle is actually in a blood-vessel.

A safer way of exploring the chest is to attach to the outer end of the tubular needle a rubber tube and funnel filled with salt solution and freed from air bubbles. As the needle is plunged in, the fluid in the funnel should be held a little above the level of the point of the needle. If serum or pus or blood is reached in the pleural cavity, the fluid will return through the salt solution, and is recognized by inserting a glass tube in the rubber tubing close to the needle. By lowering the funnel the pleural exudation can be siphoned off. If the point of the needle has penetrated the lung, no harm will come from some salt solution running into a vein.

(2) The precautions recommended when instituting an artificial pneumo-

thorax are generally sufficient; but when the lung is adherent in places to the parietal pleura and the needle enters the lung, the respiratory movements swaying the needle may cause small excursions in the manometer which may give rise to the belief that the needle has entered the pleural cavity. In any case, before any air or gas is let in, some salt solution should be run in under as low a pressure as possible. If now the needle is in the lung, the patient will make some complaint, such as of pain or tightness in the chest. Attention should be paid to even a small complaint ; the needle should at once be withdrawn entirely.

It is folly to persist after such a warning; and likewise wrong, after a definite disturbance, to make subsequently another attempt.

(3) The irrigation of an empyema cavity with a wide exit is not subject to accident so long as salt solution is used and not an irritating antiseptic. But there is a possibility of danger if an empyema sinus is injected; the lining granulations being rubbed off, the injection may enter venules, or the deep inspirations of the patient draw in air. An excision of the outer portions of the sinus, so that the whole cavity can be plugged and made to heal from the bottom is the treatment to be adopted.

(4) When exploring an exposed lung in the search for a pulmonary abscess or excavation by bronchiectasis, the entry of air into a pulmonary vein may be prevented by filling the wound with salt solution, in the same way as air embolism may be prevented when operating on the neck, in addition to keeping the needle filled with the salt solution by means of the rubber tubing and funnel.

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W. G. S.

THE SURGICAL TREATMENT OF CANCER OF THE RECTUM

The importance attached to the subject of cancer of the rectum is evident from the number of surgeons who took part in the discussions on this disease which have recently taken place in various countries. In this country the discussion was opened by W. E. Miles, by A. Schwartz in France, by A. D. Bevan in America, by Küttner in Germany, who reviewed 800 cases at Breslau, by Bull at Christiania.

It is difficult to appreciate the progress being made because of the absence of knowledge as to the origin of the disease, the different situations at which the disease commences, the variety of course which it pursues, and the return of the disease later, after removal. The individual cases are so variable that to make a statistical collection and institute a particular procedure for general adoption is to force conclusions.

There is one matter upon which all are agreed, that the majority of cases up to 90 per cent. come under the notice of the surgeon when the cancer is already irremovable. In some of these the practitioner has neglected to insert his finger into the rectum, in others a somewhat fuller examination would have furnished a diagnosis at an early stage. There remain cases in which acute intestinal obstruction is the first occasion for consulting the doctor. Special attention has been devoted to the 'combined abdomino-perineal operation', but the term has been applied in very different ways. Some procedures have consisted in making an artificial anus, and in mobilizing the bowel by dividing the peritoneum on each side; on the other hand, a very extensive operation has been done on the ground chiefly that the disease spreads at an early stage by the lymphatics to the glands of the mesorectum and to those along the iliac arteries, as well as laterally. A full trial, however, of this wide removal has disappointed expectations as regards the eradication of the disease, whilst the mortality is high. It is agreed that this operation is not suitable for old people, nor for fat patients, nor for those already suffering from some degree of intestinal obstruction unless after a preliminary colostomy. Excluding such cases, the abdomino-perineal operation of a thoroughgoing character, such as is advocated by Miles or by Schwartz, is attended by an immediate mortality of at least 30 per cent. But the more important disappointment experienced has been the frequency of failure to arrest the disease. The cases in which the disease appears at a relatively early age are not cured; the method also fails to arrest the disease in which the lymphatic glands are enlarged at an early stage. The advocates of the perineal operation combined with an artificial anus can show that this operation is free from danger, ensures a fair degree of comfort after the operation, and is followed in many cases by a long survival, supposing that the procedure is applied to suitable cases.

In view of the wide differences which characterize individual cases, it would seem wise to avoid a routine operation, to have in mind the many varieties of procedure, and to adopt the line which appears most suitable to the individual case.

1. **Perineal operations without an artificial anus.** The original operation removed the sphincter ani, exposed the patient to infection of the wound by the faeces, and left him with an unsatisfactory orifice. If the patient comes under examination at a very early stage a small ulcer may be found which involves the mucous membrane and submucous tissue only, a little distance above the internal sphincter, and the ulcer may still move over the muscular coat. Or there may be in the same situation a polypoid growth, the pedicle likewise without connexion with the muscle. It is difficult to be certain of the disease without a microscopic examination. In such a case a median incision may be made backwards through the sphincters and the lower end of the rectum; after the removal of the coccyx, the cut edges of the rectum can be held apart. The ulcer or polypoid growth is thus well exposed to view, a line can be drawn round it by the cautery, and, continuing to use the cautery, the disease can be detached from the inner surface of the muscular coat. Such a wound falls together and unites with restoration of the activity of the sphincters, whilst there is an absence of septic infection. Meanwhile the growth can be examined by the microscope, and digital examination at intervals will supply information as to freedom from recurrence.

2. **Perineal excision along with an artificial anus.** The procedure known as Kraske's operation, viz. the removal of the coccyx and lower end of the sacrum, the excision of the anus and lower part of the rectum, and the formation of a sacral anus, may be definitely condemned, because of the liability to infection of the wound and owing to the defects of the sacral anus. Whenever the anal sphincters have to be removed, an artificial anus in the abdominal wall is an essential accompaniment. The best indication for a perineal excision remains unaltered, that the finger can be passed beyond the growth, which can be moved by the finger upon the structures surrounding the rectum. The steps of the operation are the formation of the artificial anus, the excision of the coccyx and lower end of the sacrum, the cutting round the anus, the separation of the rectum from the hollow of the sacrum, the division of the levator ani, the separation from the bladder and prostate in the male, from the back wall of the vagina in the female, and the opening of the peritoneum and the pouch of Douglas.

Except in the cases in which the pelvic colon can be readily drawn down, the rectum has now to be divided well above the growth. Some cut through, then invaginate and close the end; some divide with the cautery and leave the upper end open; a longitudinal slit may be made above the level of the growth, a glass tube with a flange pushed up, and a ligature applied tightly to surround the bowel and tube below the flange. This has the advantage of controlling haemorrhage and preventing septic contamination of the wound for the next three or four days until the ligature cuts through. The peritoneal cavity can now be shut off by suturing to the bowel above the level of the ligature.

Doubt arises as to the indications for this operation when the finger can pass well beyond the growth but it is fixed in front. When in the male the fixation is limited to the capsule of the prostate and vesiculae seminales, separation may be undertaken; when the separation would involve a wound of the bladder or ureter, the disease should be considered unsuitable for removal, because the suffering of the patient will be increased by a urinary fistula. When in a woman the back wall of the vagina is involved and the sphincter ani has to be removed, the case should be considered as requiring the combined abdomino-perineal operation with hysterectomy, as described by Schwartz. If the rectum, the anus, and posterior wall of the vagina are removed solely by way of the perineum, a persistent vaginal fistula will probably form.

3. **Excision of the rectum whilst preserving the anus.** An annular carcinoma which commences well above the internal sphincter tends to produce an invagination by stretching and drawing upon the pelvic colon. The first point then for consideration is whether it is likely that the bowel above the disease can be drawn down through the anus without arresting its circulation. The freedom of the gut may be established by a bimanual examination under an anaesthetic, followed by an abdominal exploration concerning glandular enlargement. Intestine brought down to the anus, under any degree of tension, tends to slough; the ligature of the superior haemorrhoidal, and more so of the main inferior mesenteric artery above the level at which the gut is cut across, leaves the cut end without blood-supply; an excision of glands above the level at which the intestine is excised also imperils the continuation of the blood-supply. The pelvic colon, and even the ascending colon as far up as the splenic flexure, has been mobilized by dividing the peritoneum on each side, so as to allow the end to be brought down through the anus, but this procedure is not to be advised. Cases of complete restoration of function have been described, but if the pelvic colon will not come down readily, there is no object in preserving the anus, which would only obstruct drainage.

4. **The artificial anus. Colostomy. Caecostomy.** An opening of the bowel through the abdominal wall has to be done at a preliminary operation when acute or subacute obstruction has already supervened. But when the bowels can be well cleared by an aperient and an enema introduced above the growth there is no occasion to trouble the patient with a preliminary operation. The formation of the artificial anus can be followed by the removal of the growth at the same sitting.

An iliac opening in the line between the umbilicus and the anterior superior spine seems the one most often made, the incision crossing this line at right angles at the junction of the outer and middle third. If the hand has not to be passed into the abdominal cavity and the internal oblique and transversalis muscles are split, the orifice will be provided with a sphincter. The sigmoid flexure having been identified and drawn upon until the descending colon is reached, a loop of the gut may be trussed up by a rod passed through the mesentery. The most projecting part of the loop then may be punctured, and a catheter passed into the descending segment by which the rectum may be irrigated. If there is some degree of obstruction a Paul's tube may be tied into each end. The ligatures on the tubes will cut through and divide the bowel; otherwise the bowel is divided by the cautery, the rod acting as a director some time before the tenth day. The result is a nipple-like protrusion of both the proximal and distal end;

the opening being at the bottom of the fixed descending colon there is no danger of prolapse. This iliac anus has succeeded in many hands, an apparatus can be conveniently fitted; many cases have later on been able to dispense with it, and merely keep on a pad of wool.

An artificial anus has been placed in the middle in order that a symmetrically constructed apparatus may be worn. The gut being fixed at the upper end of the median hypogastric incision used for excising the rectum, a separate iliac incision is avoided.

The artificial anus has also been made in the left linea semilunaris, below the ribs on the left side, or in the groin.

There are certain cases in which a valvular appendicostomy-caecostomy should be done by passing in a large rubber catheter and invaginating the edges of the opening in the intestine. It is a great mistake to inflict a left-sided colostomy on a patient whilst the diagnosis is uncertain. Cases have been rendered miserable by it for the rest of their lives when done for what subsequently proves to be some temporary inflammatory condition such as diverticulitis. Gas and fluid faeces can be sucked back from the ascending colon, after which the colon can be irrigated from above downwards. In case of the obstruction subsiding the catheter can be withdrawn and the opening closes of itself.

Besides acute cases in which the diagnosis is not well established, there is the cylindrical form of inoperable causes, situated above the lower sensitive part of the rectum. Such a growth does not cause complete obstruction unless the caecum and colon are allowed first to become distended by gas; it does not bleed and it does not cause pain; its progress is very slow. The patient can learn to regulate his motions by means of the appendicostomy catheter, the motions are passed in a natural way, and the drawbacks attending left colostomy are avoided.

5. **The annular carcinoma causing early and complete intestinal obstruction.** This form has already been referred to as felt by the examining finger especially when accompanied by invagination of the rectum. When found by abdominal exploration two extremes may be met with: a constriction as if by a ligature without local infiltration or glandular enlargement; on the other hand, the peritoneum in the neighbourhood may already present scattered nodules. Generally obstruction supervenes before there is much local infection or invasion of the glands. Such a condition is met with at the junction between the rectum and pelvic colon. Here is perhaps the one position where a Murphy's button may be adopted. A swab on a holder, passed into the rectum, is made to push up the annular growth, which is cut out and the Murphy's button inserted, union by suture in this position being almost impossible. At the same time an appendicostomy catheter is inserted for a little while.

6. **The combined abdomino-perineal operation.** Miles summarized the description of the operation he had performed as follows: 'By this means the whole of the pelvic colon (except the part utilized for forming the colostomy), together with the whole of the rectum encased in its sheath of fascia and propria, the whole of the pelvic mesocolon, the peritoneum lining the floor of the pelvis, together with a strip on either side of the parietal attachment of the pelvic mesocolon, the whole of the levator ani muscles, the external sphincter muscles, as much as possible of the ischiorectal fat, and a wide area of perianal skin are removed'—'leaving nothing but the bones and bladder, and still recurrence happened.' Miles had treated

72 cases by his radical method; 24 died of the operation, but only 2 among the latest 11 cases, an improvement attributed to the adoption of spinal anaesthesia in combination with gas and oxygen. Of the 48 who survived the operation, 31 were traced: 3 had died of intercurrent disease, 8 of recurrence of the cancer. Of the 20 known to be alive, 16 had survived the operation more than six years.

A. Schwartz described his procedure for cancer of the rectum in women, where the disease commences about the level of the cervix uteri. He advocated in all such cases a complete hysterectomy for the special reason that the pelvic peritoneum might be accurately brought together by suture in order to definitely shut off the peritoneal cavity from below. He therefore commenced the abdominal stage of the operation by dividing the lateral and anterior attachments of the uterus, the cervix remaining connected with the rectum behind, which he removed together with the posterior wall of the vagina as far as regards at least its upper third. Generally, the pelvic colon was divided, its proximal end being fixed in the upper end of the hypogastric incision, the lower end with the mobilized rectum and uterus being crammed down into the pelvis. Over this the pelvic peritoneum was accurately united; Schwartz laid stress on this step; in order to attain such union he did not make the extensive removal recorded by Miles. He thus shut off the peritoneal cavity before turning to the perineal stage. After completing the excision of the rectum from below, he refashioned a smaller vagina by suturing from above downwards the cut margins of the anterior and lateral walls.

Schwartz had given up attempts to bring down the upper end of the bowel through an intact sphincter, for he had found that the risk of sloughing was too great. He made no attempt to close the perineal wound, having already shut off the peritoneal cavity; the open wound prevented any retention of discharges; it healed in the course of three or four months.

In the discussion which followed the reading of Schwartz's paper, Quénu reported the case of a woman on whom he had performed a limited abdomino-perineal excision with a permanent iliac anus in February 1903. She died of recurrence of the cancer in June 1920, at the age of 67, having survived the operation 17 years and 4 months. Auvray added another case of a woman who, after a similar operation in May 1911, had remained well and was working in the fields in November 1920, at the age of 62. She kept night and day a small retention band on the iliac anus. Savariaud operated in 1903 by the perineal method combined with an iliac anus on a man who was kept under observation. He served as a dissecting-room attendant until his death from recurrence of the cancer after fifteen years.

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W. G. S.

THE SYMPTOMATOLOGY AND TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM

This important and comprehensive subject was chosen for consideration by the Neurological Society of Paris at its first annual reunion in July 1920. The subject was introduced by Sicard, who directed discussion under four main headings: (1) The nature of the syphilitic virus: is this single, or, as suggested by Levaditi and A. Marie, dual ('virus dermotrope' and 'virus neurotrope')? (2) The clinical forms of syphilis of the nervous system defined according to the seat of activity of the virus (primary vascular syphilis with associated meningeal lesions and secondary parenchymatous changes, and primary parenchymatous syphilis with secondary meningovascular changes [tabes and general paralysis]). (3) Serological diagnosis of syphilis—the reactions of the cerebrospinal fluid. (4) The treatment of syphilis of the nervous system.

(1) The Nature of the Virus, Single or Dual?

Levaditi and A. Marie (*Medical Science*, 1920, **1**, 658) believe that there are two strains of syphilitic virus, a dermotropic strain that produces a characteristic primary lesion, well-marked secondary cutaneous lesions, and also pronounced tertiary, bony, and visceral lesions, but does not affect the nervous system, and a neurotropic virus, also with its own type of primary lesion, but rarely giving definite secondary or tertiary lesions like the dermotropic virus. This gives rise to syphilis of the nervous system. Each strain has, in addition, its own biological and cultural peculiarities. Sicard rejects this view on the following grounds: other organisms than that of syphilis possess strains of varying tissue affinities—for example, the tubercle bacillus and the leprosy bacillus—yet no one speaks of dermotropic and neurotropic strains. Since it appears from Levaditi and Marie's observations that the neurotropic virus gives no secondary or tertiary cutaneous lesions, it can only be transmissible during the primary stage, and if this be so the strain would soon die out with so few chances to spread. But the direct contrary is the case and nervous syphilis is increasing. Krafft-Ebing was unable to inoculate general paralytics with virus from chancres, and it is extremely unlikely that he was only dealing with neurotropic strains. Sicard himself was equally unsuccessful in two cases.

It has been said that persons infected from a single source have developed syphilis of the nervous system, yet in the recorded instances nothing is ever said as to the ultimate fate of the original source of infection in this respect, and Sicard believes that such cases are pure coincidences. He further suggests that once a strain has become established in a particular tissue it quite possibly develops an affinity for this and will grow less readily in other tissues. In conclusion, Sicard maintains that in deciding the ultimate fate of a syphilitic infection in any given case the soil is more important than the seed.

In the discussion following this opening paper there was a preponderance of opinion in favour of Sicard's view. Jeanselme and Bloch recorded three interesting cases of **cephalic chancre** followed at once by cerebral symptoms, headache, vertigo, lethargy, and intense neuralgic pains in one case, facial palsy in another, and by left-sided nerve deafness in a third. They suggested that possibly perineural lymphatic conduction to the base of the brain may have accounted for this. In discussing **racial factors** there was general agreement, except on the part of a Japanese observer, that oriental races, though extensively syphilized, rarely develop general paralysis or tabes. On the other hand, Europeans infected from such sources are as prone to either of these diseases as though infected in Europe.

(2) The Clinical Forms of Syphilis of the Nervous System.

Sicard maintains, like Head and his co-workers in this country, that there are two main forms of syphilis of the nervous system; a primary meningovascular syphilis with secondary parenchymatous lesions, and a primary parenchymatous syphilis (tabes and general paralysis) with secondary meningovascular lesions.

Primary vascular syphilis occurs when there is a general invasion of the meningeal vessels by the spirochaete—for example, during the secondary stage. An acute or subacute meningitis follows, which may be latent or may be of a severity to produce clinical symptoms. In the case of a localized invasion of the vessels. local arterial lesions result, with the production of thrombosis or haemorrhage leading to hemiplegia or paraplegia.

Primary parenchymatous syphilis. In this the spirochaete establishes itself in the nervous elements of the central nervous system and lays the foundation of future tabes or general paralysis.

There was by no means general agreement among those taking part in the discussion upon this point, and on the whole the general opinion was in favour of a fundamental pathological unity in all nervous syphilitic lesions. For example, Ravaut denies the existence of a pure primary parenchymatous syphilis, for in all cases so-called a meningeal reaction in the cerebrospinal fluid is found, even earlier than the clinical manifestations. Hence he would distinguish a *preclinical stage* of syphilis of the nervous system, for even the earliest possible diagnosis of tabes on clinical grounds is never made without a reaction in the cerebrospinal fluid being also found. The reactions in question include the cellular, albuminous, and the Wassermann reactions. He concludes therefrom that a meningeal lesion always precedes a parenchymatous one. Roussy also denies the existence of primary parenchymatous syphilis of the nervous system, for neither the morbid anatomy of the disease nor general pathological principles are in accord with such a dual nature of syphilis. The essential lesion of syphilis wherever found in the body, from the primary to the tertiary stages, is an endarteritis, and the view that syphilis of the nervous system stands on a plane apart from syphilis elsewhere is unsound. In the immense majority of cases of tabes and general paralysis meningeal lesions are to be found, while vascular lesions are never wanting. He thinks it impossible to conceive of such an organism as the spirochaete traversing the vessel walls on its way into the nervous system without leaving some tissue reaction to mark its passage. During the years before tabes or general paralysis develop, where does the spirochaete slumber in the nervous system? It could not do so in the connective tissue without producing some tissue reaction, while the highly differentiated nerve-cells certainly could not harbour it without some disorder of their functions resulting. He concludes that a primary lesion of so highly specialized a tissue cannot occur, while it is only reasonable to suppose that an organism so slow and chronic in its activity should produce a connective tissue reaction. The essential lesion of tabes, as demonstrated by Nageotte, is vascular and meningeal, and this leads to degeneration of the entering nerve-roots. There is therefore no essential division between meningovascular and parenchymatous syphilis of the nervous system.

André Leri discussed the relative positions, in respect of the site of the primary lesion, of syphilitic amyotrophy and optic atrophy respectively. Head and his fellow workers consider that the former may be produced by meningovascular as well as by central or parenchymatous lesions. Leri maintains that all cases are meningovascular in origin. For, while long-standing cases may appear to show pure parenchymatous lesions in the cord, yet it is to be remembered that the most characteristic meningovascular lesion of syphilis is a meningeal and perivascular infiltration by lymphocytes. This may be a transitory phenomenon, and on disappearing it leaves little but some sclerosis of meninges and vessels, which may well pass unperceived, leaving the parenchymatous lesions predominant in the histological picture. This is equally true of the amyotrophy of tabes. Optic atrophy, contrary to a widely accepted view, he also regards as meningovascular in origin. He bases his belief on the study of the optic nerves of 68 subjects with either tabes or general paralysis, of whom 28 had complete optic atrophy with blindness. In every instance the evidence pointed to a primary meningovascular lesion of the nerve, and the degeneration of the nerve fibres was strictly proportional to the degree of this meningovascular change. Finally, like Roussy, he maintains that syphilis of the nervous system, like syphilis elsewhere in the body, starts from a vascular lesion.

(3) The Serological Diagnosis of Syphilis of the Nervous System.

According to Sicard, there are four essential reactions in the diagnosis of syphilis of the nervous system: the blood Wassermann, the cerebrospinal Wassermann, the cell, and the albumin contents of the cerebrospinal fluid. A positive Wassermann reaction in the fluid is the only certain criterion of syphilis of the nervous system. This reaction is constantly accompanied by increase of coagulable proteins ('hyperalbuminose') and almost constantly by increased cell content. In the evolution of neurosyphilis the order of appearance of the reactions in the fluid is probably as follows: albumin, cells, Wassermann reaction, while under treatment they clear up in the reverse order, so that there may be increased cellular and globulin content with a negative W. R.

In **tabes**, even untreated cases (10 per cent.), the blood and cerebrospinal W.R. may be negative, and it is not uncommon to find it positive in the blood and negative in the fluid. Under treatment, the blood W.R. usually disappears before that in the cerebrospinal fluid, and in most cases it can be abolished in both. **In general paralysis**, on the other hand, the case is quite otherwise. The W.R. is constantly present in the fluid and there is no exception to this rule, nor can it be abolished by treatment, though this may occur with the blood W.R.

In syphilitic hemiplegia and paraplegia the cerebrospinal fluid W.R. is always positive at the onset, but may later become negative, and in these circumstances there may be a residual pleocytosis. The intensity of the infection of the cerebrospinal fluid can be estimated by comparative tests on blood and fluid. It may be said to be severe in untreated cases when the W.R. is positive in both blood and fluid, and moderate when positive in cerebrospinal fluid alone. If the reaction in the blood is rendered negative by treatment, but rapidly reappears, the infection may be considered very severe.

Sicard does not believe that these reactions in blood and fluid can ever be detected in the absence of clinical signs of syphilis of the nervous system (contrary to the views of Ravaut already quoted). Even if this be true of the blood W.R., the fluid W.R. is certainly never found unless physical signs are also present, such as Argyll-Robertson pupil, or inequality of the pupils. It is not certain whether this rule applies to isolated cell and globulin changes in the fluid. Apropos of the value of repeated lumbar punctures as a method of control in syphilitics, Sicard points out that the puncture of the theca during the active secondary stage is not free from the danger of infecting the meninges.

The puncture of a small vessel while inserting the needle might well produce such a meningeal infection. In tertiary syphilis this danger is certainly not present, but even here there are certain minor objections to subjecting a patient to this procedure. If, as he believes, clinical symptoms always antedate changes in the fluid, it should not be necessary to perform the annual or six-monthly punctures advocated by some authorities. Therefore, unless there are clinical manifestations present, lumbar puncture is not really called for.

Ravaut, with the exception already quoted, agrees in the main with Sicard. He believes, however, that the W.R. in the blood gives no certain information as to whether or not the nervous system is involved, and while the W.R. in the cerebrospinal fluid is of great value, a positive reaction may occasionally be obtained apart from syphilis if certain technical precautions are not observed.

(4) Treatment of Syphilis of the Nervous System.

Sicard gives a detailed description of his own methods, for which he makes great claims. **Indications for mercury** are cases of recent hemiplegia or paraplegia, early tabes when the patient is in good general health, and during secondary syphilis before arsenic is employed. He recommends intramuscular injections of the cyanide of mercury in doses of from 0·1 to 0·2 gr. For general paralysis and for long-standing syphilitic scleroses he regards the drug as harmful. **Indications for iodide** are the same as for mercury.

Method of administration of arsenical preparations. Sicard employs galyl, sulfarsenol and novarsenobenzol. Believing that the usual plan of giving heavy weekly doses by intravenous injection is the cause of the various untoward sequelae recorded, is less effective than the use of small doses, and, during the secondary stage, may even aggravate the nervous lesion, he recommends the use of rapidly repeated small intramuscular or subcutaneous injections. In each course a total dosage of from 5 to 8 gr. of the drug is given, beginning with doses of from 0·15 to 0·2 gr. repeated daily or on every other day. The drug is dissolved preferably in an oily medium or in an aqueous solution of glucose. Sterile distilled water is quite satisfactory, though possibly it makes a less completely painless injection. The amount of solvent used is 2 c.c. Apparently several French chemical firms put the drug on the market ready made up in one or other of these media. He gives general indications for the treatment of the various clinical forms of neurosyphilis.

In every instance treatment is controlled by examination of the reactions in blood and cerebrospinal fluid. The various complications and sequelae of arsenical treatment are described by Sicard; erythematous eruptions, jaundice, abolition of tendon reflexes, anaphylactic reactions, and 'azotémie', but he claims that all these can be avoided by the method of repeated small doses. Any signs of intoxication are treated by cessation of treatment and the adminstration of magnesium and iron salts.

Intrathecal therapy with arsenic and with salvarsanized serum is discussed in all its variations, but Sicard expresses himself as unconvinced of its value, while he definitely condemns subarachnoid cerebral treatment as futile.

Babinski expressed himself as convinced of the value of long-continued mercurial treatment of tabes, by means of injections of calomel.

Souques also agrees that mercury is of value in tabes at every stage, and that better results are not obtained by the addition of novarsenobenzol, but he has never seen return of the reflexes, of pupillary reactions, or the actual cure of tabes, while certain cases cannot even be stayed in their progress downward by this treatment. The symptoms that respond to this form of treatment are pains, paraesthesiae, and ataxy.

Milian agreed with Sicard that intraspinal therapy is useless; on the other hand, he was also of opinion, as was Ravaut, that Sicard's method of repeated small doses is inadequate and is no more free from complications than other methods. According to Milian the ideal dosage is 1·5 gr. of novarsenobenzol per kg. body weight of the subject. The dose thus estimated is repeated every five days for five doses. A six weeks' course of mercurial injections then interrupts the arsenic, which can be resumed subsequently, and the process continued for several months.

Tinel recorded the results of antisyphilitic treatment of 53 cases of tabes and general paralysis at the Salpêtrière from 1912 to 1914. In the case of the tabetics improvement was obtained, but was not permanent unless treatment was continued. As for the general paralytics, most of them appear to have died in the natural course of events during the period 1914–19.

The report of this discussion occupies 140 pages of the *Revue Neurologique.* It contains case reports, technical details of diagnostic and therapeutic methods, and much diverse opinion. Unhappily, therefore, it is not readily capable of condensation, nor can any other than the most general conclusions be drawn from it. However, the bulk of opinion among those taking part seems to justify the following general conclusions. (1) That the virus of syphilis is probably single and not dual and that there is no conclusive evidence of the existence of a neurotropic strain. (2) That there is but a single form of syphilis, that probably there is no primary parenchymatous syphilis, and that in the nervous system as elsewhere in the body the essential syphilitic lesion is in the vascular system, the meningeal and parenchymatous lesions being secondary or associated. (3) That all forms of neurosyphilis, including tabes and general paralysis, should be given careful antisyphilitic treatment. However, general paralysis offers but little hope of improvement, though tabes responds on the whole more favourably. As to the details of treatment, opinions differed, while intrathecal therapy does not appear to have obtained an influential following in France. F. M. R. W.

Sicard and others. Discussion at the Meeting of the Neurological Society of Paris in July 1920, *Rev. neurol.* 1920, **37**, 612–748.

ABSTRACTS

SURGERY

Cividali, A. Contributo alle diagnosi della fistole gastro coliche. [**Diagnosis of gastro-colic fistula.**] *Policlin.*, 1920, **27**, 301.

Cividali's paper consists of an analysis of the records of 106 cases of gastro-colic fistula. The commonest cause of this condition is carcinoma of the stomach ; less frequently simple ulcer of the stomach ; rarely carcinoma or tuberculous disease of the transverse colon. One case only of indirect communication between colon and stomach through a gastro-enterostomy loop, is mentioned, that of Urrutia (*Clin. mod.*, 1912, p. 251).

Among the numerous symptoms of gastro-colic fistula, three are of prime importance: (1) Faecal vomiting, apart from symptoms of obstruction; (2) frequent diarrhoea, ultimately lienteric ; (3) when these two symptoms are present, the impossibility of distinguishing vomited matters from faeces.

Other important symptoms are: rapid wasting; sudden cessation of the daily vomiting, and the appearance of diarrhoea in place of an habitual constipation; a faecal odour of the eructations and vomited matters; the possibility of distending the stomach per rectum; the appearance in the stomach of substances (methylene blue) introduced per rectum ; the recovery in the faeces, before the termination of gastric digestion, of coloured matters introduced by the mouth ; and the presence of hydrochloric acid and pepsin in the faeces.

The grouping of these symptoms in individual cases varies, and depends on such factors as the condition of the pylorus, the width and form of the fistula, which in some cases may be permeable in a direction from the stomach to the colon only, in others in the opposite or in both directions.

Faecal vomiting may be absent when the aperture of communication, owing to peculiarities of form, size and position, obstructs the ready passage of food into the colon ; and in such cases, when the stomach is full, its repletion interferes with the reflux from the colon. It may be absent when the aperature is large, the passage of material being then more easy from the stomach to the colon than in the reverse direction ; also when a valve-action exists, or with very narrow apertures, in which case, however, a faecal odour of the stomach contents will be present. Diagnosis is often difficult without a radiological examination, and this should be made by means not only of a bismuth meal, but also of a bismuth enema, which is necessary for detecting a fistula which is permeable from the colon to the stomach only. The radiological signs of gastro-colic fistula may be summarized as follows:

A. **After a bismuth meal.**

1. Obscurity of a portion of the outline of the stomach.
2. Evidences of perigastritis, with diminished mobility of the organ.
3. Incomplete filling of the stomach.

4. A bismuth shadow situated beside the stomach, visible immediately after the meal.

5. The appearance of part of the bismuth in the descending and sigmoid colon shortly after the meal, with its absence from the ascending and proximal part of the transverse colon.

6. The possibility of transferring the bismuth from stomach to colon or *vice versa,* by means of palpation.

7. The associated presence of bismuth in the small intestine and in the distal portion of the colon, while the intermediate parts are free.

B. **After a bismuth enema.**

1. The presence of bismuth in the stomach.
2. The possibility of forcing bismuth into the stomach by palpation.
3. The presence of bismuth in the small intestine.

C. **Injection of air per rectum.**

Distension of the stomach occurring during the insufflation.

These signs cannot all be elicited in every case, but they have all proved of value in particular instances. T. W. P. L.

Biancheri, T. M. Le lesioni traumatiche del carpo. [**Traumatisms of the carpus.**] *Chir. degli organi di mov.*, 1920, **4**, 347.

Biancheri gives the results of an experimental study of dislocation and fractures of the carpus, undertaken mainly with the intention of testing the value of X-rays as a means of accurate diagnosis. The injuries were produced on 50 dead bodies by means of a wooden mallet, the hand being placed in various positions. Apart from mere detachment of cartilage, which naturally would escape detection, the lesions were not revealed by the X-rays in five cases. In fracture of the neck of the os magnum the surface of fracture is either oblique from before backward and upward, or, if horizontal, the fractured surfaces are dentate and fit together accurately; moreover the lateral projection is of no assistance owing to the superposition of shadows. Superposition of shadows may also obscure the presence of small fragments, and even if these are visible it may be impossible to identify the bone from which they have been detached. Moreover, fissures connecting fractures with the joint cavities are at times invisible.

After describing his experiments in detail, Biancheri discusses fractures and dislocations of the carpus systematically, appending a very complete bibliography of the subject. He classifies dislocations under the following headings: (1) Radio-carpal, which may be posterior (complete or incomplete) or anterior (almost invariably complete); (2) Intercarpal, anterior or posterior, and in either case of rare occurrence; (3) Dislocation of individual bones (scaphoid, trapezium, pisiform); (4) Perilunar. In the last-named type the semilunar bone is displaced in relation to the bones on either side of it. The lesion may be isolated or combined with fracture of the styloid process of the ulna or radius, fracture of the pyramidal, scaphoid or os magnum, or of the anterior margin of the semilunar itself. Following Donati, Biancheri recognizes four types of perilunar dislocation. (1) Anterior, the semilunar being displaced forward on the radial articular surface; (2) Posterior, the semilunar retaining its normal relation to the radial surface, while the remaining carpal bones are dislocated backward; (3) The two preceding types combined; (4) Posterior displacement of the carpus, associated with fracture of the scaphoid, the semilunar and the proximal fragment of the scaphoid retaining their normal relation to each other and to the radius, while the distal fragment of the scaphoid is displaced backward with the rest of the carpus. Perilunar dislocation may be produced directly or indirectly, as in a fall on the palm with the hand in over-extension (rarely in forced flexion), or through the counteraction of the handle of a motor. A description of a case illustrating this type of dislocation, which came under Biancheri's observation, is given, with figures and radiograms. The prognosis in these cases is grave if reduction cannot be effected, since nervous disturbance is likely to persist and may lead to muscular atrophy of the whole limb. Attempts at reduction, the success of which largely depends on the date at which they are undertaken, are justified if the radiogram shows clearly that the semilunar bone has not lost its normal relations to the radius, though some surgeons consider that a mere rotation of the bone to an extent of not more than 90° should not be taken as a contra-indication. The hand is placed in a position of over-extension, the semilunar bone being immobilized by moderate pressure in order to prevent its displacement; the over-extended hand is then drawn forcibly in a distal direction and rapidly brought into the flexed position. Extirpation of the semilunar bone, with or without the fragments of the scaphoid and pyramidal, in case of fracture of these bones, should be resorted to in all cases in which compression of nerves or severe functional loss in the limb are present. The results are good, but success depends largely on the early performance of the operation. In old-standing cases, with partial or total ankylosis, more or less extensive resection of the wrist is necessary. T. W. P. L.

Torraca, L. La circolazione sanguigna dei nervi isolati. [**The circulation in isolated nerves.**] *Chir. degli organi di mov.*, 1920, **4**, 279.

In cases where it was found to be difficult to approximate the severed ends of wounded nerves, Delorme, in order to obtain greater extensibility, recommended the isolation of the nerve-trunk in a considerable part of its length. Some doubts have been expressed as to the degree of danger to the vitality of the nerve involved in this procedure, and Torraca's experiments were designed to ascertain how far the intrinsic vascular supply could be relied upon to maintain the vitality of the nerve, apart from any collateral sources of blood-supply. The experiments were made on dogs, the sciatic nerve being isolated in its whole extent and denuded of epineural connective tissues as completely as possible. In order to exclude the formation of collateral channels the nerve was protected from the surrounding cellular tissue by an indiarubber sheath. A merely transitory paralysis followed the operation, and the animal rapidly regained full powers of movement. On microscopical examination Torraca found that the more important arterioles accompanying a normal nerve-trunk run in the connective tissue surrounding the nerve-bundles, and from these, branches are given off which, with free anastomosis, penetrate the nerve itself. In no case was it found that the isolation of the nerve had involved the removal of the main arterioles, although the superficial connective tissue had been dissected away with all possible completeness, more thoroughly, in fact, than would be the case in the operation in man. A marked increase in the calibre of the larger arterioles was also observed, amounting to double their normal diameter. This change, however, appeared to be mainly due to the presence of the rubber sheath, since in operations performed without this the increase was scarcely appreciable. Torraca concludes that the intrinsic circulation of an isolated nerve is amply sufficient to preclude all danger of necrosis.

T. W. P. L.

Serafini, G. Esteriorizzazione di un' ansa del tenue sotto la cute dopo enterorrafia. [**Subcutaneous exteriorization of the intestine.**] *Arch. ital. di chir.*, 1920, **2**, 339.

Summary. Wound and prolapse of intestine treated:

First, by suture of the wounded intestine with fixation in the open wound of the abdominal wall.

Secondly, suture of the skin of the abdominal wall, establishing a ventral hernia of the intestine.

Thirdly, cure of the ventral hernia.

The patient, a boy aged 14, was thrown violently forward from his bicycle seven hours previously, the handle of the machine wounding the abdominal wall. Part of the great omentum had prolapsed through the wound, which was 4 cm. in length and situated to the left of the umbilicus. The prolapsed omentum was resected and the abdomen opened, a small quantity of foetid liquid escaping. The small intestine was found to be wounded transversely and detached from the mesentery for a short distance; the mucosa was extroverted. The bowel was congested and covered with fibrinous exudate for some considerable distance around the wound. The peritoneum was cleansed and the wounds in bowel and mesentery sutured. The abdominal wound was then closed, leaving a transverse opening inferiorly for a gauze drain, and above this an ample opening for the wounded loop of intestine, which was fixed in place by silk stitches.

During the first two days the patient suffered from pain and vomiting, but these symptoms ceased on the third day. On the eighth day the bowels acted normally. On the tenth day it was decided to cover the exteriorized bowel with skin. The skin on either side of the loop was dissected up widely, several short transverse cuts were made in the muscular tissue bounding the abdominal opening, and the skin was then drawn over the bowel and sutured, the folds being sufficiently lax to preclude undue pressure. A small drain, inserted inferiorly, was removed on the fourth day. The patient subsequently took his food well, suffered no pain, and had regular action of the bowels. Seven weeks later the loop was returned to the abdominal cavity, an incision being made on the outer aspect of the swelling. The intestine had become partly adherent to the skin and subcutaneous tissue, but the adhesions were broken down readily. The mesentery was separated without difficulty from the margin of the aperture, but the intestine adhered somewhat closely and a small flap of its sero-muscular layer became stripped up and required to be replaced with a few fine silk sutures. Within the abdominal cavity, a few loose adhesions were readily broken through and the loop of bowel returned. The patient recovered well and remained free from symptoms.

Exteriorization was originally designed as a temporary measure in cases where surgical treatment of the bowel was contemplated. Later, Ferrarini (*La Clinica Chirurgica*, 1911) studied the conditions under which permanent exteriorization could be rendered possible. On the intestine subcutaneously exteriorized Ferrarini successfully carried out various operations—enterostomy, lateral anastomosis, resection with end to end anastomosis, lateral anastomosis with subsequent resection. In addition to affording control in operative treatment, the method enables the surgeon to satisfy himself as to the degree of vitality possessed by the bowel in cases, such as strangulated hernia, where any doubt exists. It may also be adopted advantageously in cases where it is necessary to render the exteriorized bowel aseptic.

With regard to the indications in his own case, Serafini remarks that the septic condition of the loop and the lacerations, involving both intestine and mesentery, rendered it imprudent to return the bowel immediately. Although it could not be asserted that this would necessarily have been attended with untoward results, a possible dangerous lowering of the vitality of the intestine made the forecast doubtful. T. W. P. L.

Stoppato, U. Proiettili nei corpi vertebrali lombari senza lesione midullare. [**Projectiles in the lumbar vertebrae without lesions of the cord.**] *Chir. degli organi di mov.*, 1920, **4**, 123.

Impaction of a projectile in the body of a vertebra without any associated injury of important organs and of the spinal canal can hardly happen elsewhere than in the lumbar region. It is possible in this region if the projectile approaches from the side and enters somewhat posteriorly to the mid-lateral line, passing inward and forward in a horizontal plane. Ten cases of this kind have been described. The fragment (usually shrapnel) may be impacted in the body of the vertebra or in the intervertebral disk, and generally a single vertebra only is involved. The symptoms are not as a rule definite enough to enable a diagnosis to be made without the assistance of the X-rays. The presence of a projectile in the intervertebral disk may, however, be suspected, account being taken of the direction of the track, when marked lordosis exists and flexion of the trunk is impossible. In one of Stoppato's cases the X-rays showed the fragment impacted in the disk between the bodies of the third and fourth lumbar vertebrae, and the vertebral bodies appeared to be driven apart anteriorly. Flexion was impossible, but this symptom may also be present when the projectile is impacted in the body, and in one case appeared to be due to the involvement of more than one vertebra in the fracture. Difficulty in walking and pain in the lower limbs were noted in three cases, without any evidence of encroachment on the spinal canal. In two cases there was some degree of rigidity and tenderness in the upper half of the abdomen. Tenderness on pressure over the spinous process of the injured vertebra is recorded in one case only, but the symptom was apparently not sought for in all cases. The impacted fragment may remain quiescent in the body of the vertebra, producing more or less severe derangements of a mechanical nature; or it may give rise to osteomyelitis with the formation of fistulae and abscesses. In Taddei's case a psoas abscess formed on the side opposite to the aperture of entry of the projectile.

In extracting the fragment the posterior route, consisting in laminectomy and lateral displacement of the spinal cord and theca, is to be avoided, unless there is a suspicion that the fragment projects into the spinal canal.

Extraction by the lateral route may be performed by the method of Treves or that of Fontan. In the former the incision (8–9 cm.) follows the outer margin of the extensor muscles, the fascia on the hinder aspect of the muscles is opened and the mass retracted towards the middle line. At the transverse processes the anterior layer of the aponeurotic sheath is incised and the attachments of the quadratus cut through. The psoas muscle, thus brought into view, is partly separated from the bone. The method necessitates working at an inconvenient depth and the possibility of wounding the lumbar arteries and nerves.

Other surgeons have used a modification of Treves's operation, placing the incision more laterally, as in the operation of lumbar nephrectomy. The posterior layer of the perirenal fascia is opened freely and the peritoneum reflected inward with the descending colon and ureter. At this stage of the operation Taddei derived great assistance from a sound passed into the fistula. The sound was cut down on as deeply in the wound as possible, and by gradually advancing it and continuing the incision over it the body of the vertebra was finally reached. Without some such assistance as this there may be a difficulty in reaching the vertebral body by this method. Ingianni experienced a failure of this kind, and only succeeded in extracting the fragment after dilating the track and using one branch of a Hegar's forceps.

In Stoppato's opinion the best method is that of Fontan. In this the body of the vertebra is reached by resecting one or two of the transverse processes. The patient is placed in the ventral position with a cushion under the abdomen to correct the lordosis. An incision of 12 cm. is made one finger-breadth external to the line of spinous processes and carried down to the lamina of the injured vertebra. The tubercle of the transverse process is then located and immediately external to it, about a centimetre and a half deeper, the flat posterior surface of the transverse process. The process is severed at its base with a chisel and removed after separation from its soft attachments. The periosteum is then raised from the body of the vertebra. Subsequent stages of the operation are greatly facilitated if controlled by the use of X-rays, the patient being placed in the lateral or ventrolateral position. The fragment is extracted with a sharp spoon.

In recent cases it is sufficient to remove one transverse process only; in older cases, in which active osteomyelitis may be present, the removal of two processes may be necessary in order to afford sufficient drainage and permit of the complete removal of the diseased tissues.

T. W. P. L.

NEUROLOGY

Loewe, L., and **Strauss, I.** **Studies in epidemic (lethargic) encephalitis.** *J. Infect. Dis.*, 1920, **27**, 250.

The authors find that the Berkefeld filtrates of brain material, naso-pharyngeal swabs, and nasal washings from cases of epidemic encephalitis produce the typical lesions of the disease in rabbits and monkeys. Spinal fluid and blood are also capable of producing the disease in this way. Many of the infected animals die with the typical clinical picture of lethargic encephalitis.

By means of Noguchi's ascitic-tissue culture methods they have succeeded in cultivating a minute filterable organism. This is seen as clumps of minute globular bodies with Brownian movement. Young cultures of this are Gram-positive. It is obtained from the brain, nasopharyngeal mucosa, cerebrospinal fluid, and blood of cases of the disease in man, and from inoculated animals dead of the disease. The organisms thus recovered from rabbits are virulent for other rabbits. Epidemic encephalitis differs from poliomyelitis in that rabbits are susceptible to infectious material obtained from the former disease, but not to that obtained from the latter. On the other hand, monkeys are more susceptible to poliomyelitis than to encephalitis. The cerebrospinal fluid from cases of poliomyelitis is innocuous to both rabbits and monkeys, but that from encephalitis is capable of producing the disease in both. F. M. R. W.

Harvier, P., et **Levaditi, C.** Virulence des centres nerveux dans l'encéphalitique six mois après le debut de la maladie. Virus encéphalitiques attenués. [**Infectivity of the nervous system in encephalitis six months after the onset of the malady.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, **36**, 1487.

In January 1920 the patient, a woman of 38, was taken ill with fever, headache, pains in the limbs, asthenia, and sleeplessness. From this date until April she remained asthenic, exhausted, sleepless, and giddy. She also complained of constant painful muscular cramps. She was not lethargic and showed no paralyses. From April until the time of her death in June she was subject to attacks of fine tremor of limbs and jaw. This had a rhythm of 30 to the minute. There were, in addition, generalized muscular rigidity and a mask-like facies, and speech was slow and monotonous. There were no cranial nerve palsies, lethargy, mental defect, or sensory or reflex changes. The cerebrospinal fluid contained no excess of cells and the Wassermann reaction was negative. Somnolence appeared as a terminal symptom. A diagnosis of the paralysis agitans type of lethargic encephalitis was made. Microscopic examination of the brain revealed the typical lesions of the disease, namely, perivascular infiltration, most marked in the substantia nigra and neighbourhood.

Emulsions of grey matter from the basal ganglia and subthalamic region were injected into rabbits intracerebrally. Both the inoculated animals developed the disease after a long incubation period and died. The usual lesions were found in their brains.

The authors draw the following conclusions: that the virus of the disease remains active in the brain for long periods, but becomes attenuated. They contrast this with the rapid disappearance of the virus from the nervous system in poliomyelitis.

These observations are therefore important as indicating the distinct identities of encephalitis lethargica and poliomyelitis. They also show that it is reasonable to regard the prolonged motor manifestations of this disease, more particularly the involuntary muscular contractions and movements, as irritation phenomena and not as sequels. F. M. R. W.

Marie, P., et **Lévy, G.** Le syndrome excito-moteur de l'encéphalite épidémique. [**The excito-motor syndrome of epidemic encephalitis.**] *Rev. neurol.*, 1920, i, 513.

Involuntary movements and muscular contractions form an essential feature in the symptomatology of epidemic encephalitis; Marie and Lévy group them together as the excito-motor syndrome. This is seen under very widely varying conditions; it may occur as an initial but transient manifestation of the disease, it may be present throughout, it may develop during the second week, or not until weeks and even months after apparently complete recovery from the acute illness. The present paper is particularly concerned with the syndrome in the two last-named circumstances. Cases have been recorded in which one or more of the motor symptoms included in the syndrome have been the sole clinical manifestations of the disease: such are the acute fatal choreiform and myoclonic forms.

The movements included in the syndrome are classified as follows: (1) **Choreiform movements,** generalized or unilateral, fine or coarse. In general they do not show the same degree of wildness or disorder as the movements of Sydenham's chorea, but are more ordered and rhythmical in character. They may be of great amplitude, or fine, a sort of miniature chorea ('petites mouvements choréiques généralisés' and 'chorée salutante rythmique'). (2) **Slow ample rhythmical movements of the proximal segments of the limbs** ('oscillations bradycinétiques'). (3) The so-called '**myoclonic movements**' of Sicard. (4) **The paralysis agitans form,** which the authors divide into the 'forme fruste' in which there is tremor, and the 'forme progressive' in which there is great general rigidity but no tremor. This type of the disease has been described by Marie and Lévy in an earlier paper (*Medical Science*, 1920, **3**. 252). (5) **Localized rhythmical movements of the muscles of the face and jaw.**

When this syndrome occurs as the sole manifestation of the disease, or its appearance is delayed and no definite symptoms of an acute illness have preceded it, the diagnosis is particularly difficult, since we have no bacteriological or serological criteria; moreover, the excitomotor syndrome is usually unaccompanied by other signs of nervous lesion, such as paralyses, reflex or sensory changes.

In investigating the history of cases presenting one or other feature of the syndrome the occurrence of the well-recognized symptoms of the disease should be sought for; namely, lethargy, ocular paralyses, pyrexia, and sleeplessness, and if no history of such an initial acute illness be obtained ('l'episode primitif encéphalitique') the following minor symptoms may confirm the occurrence of a mild attack ('episode primitif fruste'): an onset of an illness with occipital headache and painful rigidity of the neck accompanied by slight fever and nocturnal delirium; disturbances referable to the muscles of mastication, such as difficulty in opening the mouth fully, tremor of the jaw, chattering of the teeth; and neuralgic pain in the distribution of the fifth nerve; attacks of facial spasm; excessive salivation; slowness and difficulty in articulation; a sense of constriction of the throat with difficulty in breathing and swallowing; frequent attacks of yawning or of hiccough; slight painful swelling of joints, and, finally, neuralgic pains of root distribution and painful muscular cramps.

One or more of these symptoms associated with slight signs of general infection indicate the occurrence of the initial infection.

The authors do not concern themselves with the pathogenesis of these symptoms, but confine themselves to purely clinical considerations.

F. M. R. W.

Rivers, W. H. R. Instinct and the unconscious. *Cambridge Medical Series,* University Press, Cambridge, 1920.

Dr. Rivers's work is of importance from several points of view. He has approached the questions of psycho-pathology from the side of biology and from the side of organic neuro-physiology, and although all his conclusions will not be agreed with, it is advantageous that these matters should be attacked from an aspect which is not that of clinical medicine, especially from an aspect which has nothing to do with 'cures'. The great question in psychology, as has many times been said, is the doctrine of the unconscious, and of course the process by which constellations of ideas come to the unconscious; the process of repression resulting in the condition of suppression. The author has produced a large number of biological examples showing the value of suppression for the satisfactory performance of many instinctive reactions. One of the reactions to danger is that of immobility. It is not an aggressive reaction but is an alternative to flight. The kind of animal which employs it is also the kind which may exhibit the reaction by flight; but if the former reaction is selected there must be no trace whatever of the latter. The slightest movement would utterly spoil the reaction and render it valueless. Here, then, is an example of the utility of suppression and, furthermore, one where incomplete suppression would be a disadvantage. The importance of the latter observation will appear presently. This example serves Dr. Rivers also to emphasize his view that the hallmark of the instinctive reaction is that it shows in its primitive form the all-or-none principle. It is perhaps characteristic of the academic pyschologists that they have an overwhelming desire to define and be precise where the clinician feels that absolute precision is not possible or indeed altogether desirable. Those whose lives are spent between the laboratory and the desk seem themselves to have suppressed all notions of the vague indefinite borders which constantly obtrude themselves before those whose knowledge is derived from patients only; and doubtless this suppression has its advantages, for without it they would not achieve those Platonic ideals with which their books are filled. It is profitable, therefore, that we should get some clear though impossible ideal presented to us of what an instinct is, though we shall never meet with one in practice, never be able to say just where instinct ends and intelligence begins.

With the growth of intelligence the purity of the all-or-none principle is no longer found; the reactions become modified. Dr. Rivers endeavours to show that hysteria may be regarded as a modified instance of the reaction by immobility. For hysterical paralysis this may be true, but the author is somewhat unfortunate when he tries to make this explanation cover the phenomena of hysterical convulsions. He states frankly that his acquaintance with civilian convulsions is not wide enough to let him be dogmatic about them, but he says further that in the military cases the convulsive attacks were not characterized by violent convulsive movements but rather by a more or less complete immobility. It is quite true that such attacks were often observed, even as they have been in civilian cases before the war, but it is also true that military cases, with movements so violent that the patient's friends felt constrained to hold him down, were common. Apart from generalized convulsions, too, there were all sorts of curious rapid movements of a localized nature which persisted for months, which could by no stretch of imagination be included under any kind of formula which implied immobility. Dr. Rivers's view, however, is interesting, and it is likely that some of these phenomena were examples of a partial reaction of flight or of defence, so that if the view be extended only a little it need not be abandoned. It is also probable that hysteria does not represent one psychological condition, but that its origins, like its symptoms, are manifold.

Apart from the recurring accident of danger, Dr. Rivers shows that suppression is of great value in the life-history of any animal. One of the obvious examples he takes from the butterfly. How inconvenient if it should remember in its rapid flight the slow torpid movements of its caterpillar stage. Similar advantages accrue to us from our complete suppression of infantile experiences.

Dr. Rivers had drawn a useful distinction between the idea of dissociation and that of suppression. The former word should be employed only when there is independent consciousness. Suppressed ideas have no consciousness, dissociated ones have a consciousness alternating with that of the ordinary personality. He has furthermore enriched the vocabulary with a word of real value, viz. the word 'unwitting'. It is commonly said that ideas are suppressed 'unconsciously'. As they are suppressed into the unconscious, this might give rise to the implication that their arrival there was due to some action of the unconscious, whereas the belief is that it is an active process taking its origin above. Some different word is therefore called for, and 'unwitting' appears to meet this want exactly.

For the clinician the importance of Dr. Rivers's work lies perhaps in his insistency that suppression is a normal and often a salutary process. Lip service to such a view is given in the Freudian literature, but opposed to it is the principle that analysis cannot be too deep. The impression which one not in the inner circle gets from the literature is that when psycho-analysis fails it is because it has been partial, because there is still dammed-up energy locked up with complexes which is causing symptoms. Here and there one does come across the admission that it is when repression is beginning to fail that the symptoms ensue, but the orthodox view probably is that all repression is bad. If it be only partial repression which is disadvantageous the work of the analyst will be shorter than if the other view be correct; and if completely buried complexes which have no associative connexions with consciousness are of no clinical importance much pain will be spared to patients. T. A. R.

Foix, C. Syndrome de la paroi externe du sinus caverneux. Ophtalmoplégie unilatérale à marche rapidement progressive. [**Syndrome of the outer wall of the cavernous sinus: rapidly progressive unilateral ophthalmoplegia.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1920, 3e sér., **36**, 1355.

Foix reports two cases of tumour, in which growth invaded the posterior wall of the sphenoidal sinus, giving rise to a rapidly progressive paralysis of the sixth, fourth, and third nerves on one side, and to neuralgic pain in the distribution of the ophthalmic division of the fifth nerve. All these nerves lie in the outer wall of the cavernous sinus and were compressed by the enlarged and infiltrated bone. In the first case the primary growth was in the mediastinum, with secondary deposits in one adrenal body and in the hypophysis. The last-named deposit had infiltrated and enlarged the sphenoid in front of the sella turcica, thus causing compression of the sinus and of the structures in its outer wall.

The second case was one of hypophyseal tumour infiltrating the bone in the same situation. In both cases the ophthalmoplegia was a terminal phenomenon of rapid onset and development. Foix speaks of this as 'the syndrome of the external wall of the cavernous sinus'. When syphilis and orbital tumours can be excluded it indicates a lesion of the sphenoidal sinus or of the pituitary body. F. M. R. W.

Mallory, F. B. The type cell of the so-called dural endothelioma. *J. Med. Research*, 1920, **41**, 349.

The generally adopted classification of tumours according to the type cell from which they arise has not been applied to dural endothelioma, with the result that its relation to other forms of tumour, and the range of variations in the cellular character of the tumour have not been elucidated. The current view is that this tumour arises from the endothelial cells lining the inner surface of the dura (the subdural space). Mallory has carried out an examination of thirty endotheliomata. In one type (cellular type) the predominating cells are large and flattened, in the second (fibrous type) they are spindle-shaped. In both there is a marked tendency to the formation of whorls, and the stroma is scanty. The cells are surrounded by delicate fibroglia fibrils and by collagen and elastic fibres in varying degree. Where the growth invades the dura, the cells of the latter are stimulated to growth and form a coarse stroma for the cells. In the whorls the large or the spindle-shaped cells may predominate, or there may be concentric layers of intercellular substance round a central point. Fibrous whorls are most common and arise from the inclusion of fibroblasts in cellular whorls.

The arachnoid differentiates early in embryonic life from the mesenchyma surrounding the brain and cord, and it separates the pia from the dura. The clefts which form as it separates from the pia later become the cisternae of the subarachnoid space, which is lined by fibroblasts alone. Where it separates from the dura, the inner surface of this is also lined by fibroblasts and there is no dural endothelium. The cleft is the subdural space. As the arachnoid develops, its fibroblasts acquire histological characteristics peculiar to it. On its external surface patches of endothelial cells form and cause local thickenings of the membrane.

With advancing age these surface cells multiply in foci and form cellular buds which may show a whorl formation. There may be dural fibroblasts in these buds, and then fibrous whorls with numerous elastic fibrils are produced. When the cells in the buds differentiate fibroglia, collagen and elastic fibrils are formed, and in this way the arachnoid becomes thickened. The buds of proliferating arachnoid cells show from their earliest stage a marked tendency to invade the dura, pressing its fibrous strands apart. When the cells secrete intercellular substance the arachnoid villi and Pacchionian bodies are produced. If the invading cells take on a malignant character, a so-called dural endothelioma results. The stroma and blood-vessels of this are provided by the fibroblasts of the invaded dura. The growth should, therefore, be regarded as an **arachnoid fibroblastoma.** The tumour may be of rapid or of slow growth, and may or may not contain whorl formations. When slow growing, the cells differentiate and produce] fibroglial collagen and elastic fibrils. Such a tumour can invade the dura and tissues external to this, but it never invades the arachnoid membrane from which it has arisen.

The perineurium is probably analogous in origin with the arachnoid, but is not an outgrowth from this. It has no undifferentiated outer layer of proliferating cells, nor is it separated from endo- or epineurium by clefts. It is most highly developed in the stratified sheath of the Pacinian corpuscle. Tumours frequently arise from it (neurofibroma, fibroma molluscum). They have certain histological features differentiating them from arachnoid fibroblastomata, and they differ also in their tendency to invade nervous tissues, as in plexiform neurofibroma.

Mallory terms these tumours **perineural fibroblastoma.** The ordinary auditory nerve tumour belongs to this group. Nerve fibres and neuroglia fibrils are sometimes found in an auditory tumour because the tumour invades the nerve in which both are normally found. In connexion with this important paper the reader is referred to Cushing's observations on the arachnoid villi (*Medical Science,* 1920, **3,** 160.) F. M. R. W.

Rizzo, C. Rigidità pupillare e ganglio ciliare. [**The ciliary ganglion and inactivity of the pupil.**] *Arch. biol. norm. e patol.*, 1920, **74**, 1.

With regard to the seat and nature of the lesion underlying the Argyll-Robertson pupil (alone, or associated with inactivity to accommodation), Marina and others have asserted that in this condition the cells of the ciliary ganglion are reduced in number, pyknotic, and show chromatolysis, and that the myelin sheaths of the ciliary nerves are degenerated. André-Thomas was unable to confirm this from the investigation of three cases.

Rizzo's observations confirm those of André-Thomas. He examined the ganglia from nine normal subjects, from eight general paralytics and one tabetic with Argyll-Robertson pupils, from two general paralytics with totally inactive pupils, from one with defective reactions to both light and accommodation, and finally from one general paralytic with normal pupils. In the ganglia of paralytics and tabetics he failed to find any noteworthy degeneration of the nerve-cells, though a few cells showed some chromatolysis and swelling of the cytoplasm which were obviously acute and recent lesions attributable to the intercurrent illness which caused death. There was no evidence of any connective tissue reaction, nor of cicatrices indicating the disappearance of cells. The roots of the ciliary ganglion, the short ciliary nerves, the nerve plexus of the muscle of Brucke, and the nerve filaments of the iris and cornea were all normal in every case. An exudate of lymphocytes and plasma cells was constant in the ganglia of general paralytics.

Certain histological details of the normal ganglia were noted. The nerve-cells are of two kinds, large and small—the former four or five times larger than the latter, which are for the most part situated at the periphery of the ganglion. The pigment also is of two kinds, one showing the reactions of the pigment of the substantia nigra, the other being the ordinary lipochrome pigment. The former is scanty, does not increase with age, and is found exclusively in some of the small cells; the latter appears later, increases with age, and is found in the large cells only, especially in the diseased cases. T. W. P. L.

Denis, W., and **Ayer, J. B.** **A method for the quantitative determination of protein in cerebrospinal fluid.** *Arch. Int. Med.*, 1920, **26**, 436.

The method gives the total protein to within approximately 5 per cent. Into a test tube of about 4 c.c. capacity is put 0·6 c.c. of cerebrospinal fluid. To this is added 0·4 c.c. of distilled water and 1 c.c. of a 5 per cent. solution of sulphosalicylic acid. The contents of the tube are mixed by inversion and allowed to stand for five minutes. The suspension is then compared in a small Dubosc colorimeter with a standard protein suspension. The latter is prepared by mixing 3 c.c. of a solution containing 0·3 mg. protein per c.c. and 3 c.c. of 5 per cent. sulphosalicylic acid solution.

The protein solution is prepared from fresh human serum. 20 c.c. of this is mixed with 200 c.c. of 15 per cent. sodium chloride solution and the mixture filtered. The total nitrogen of this is estimated by the Kjeldahl method. Such a solution will keep for three months in an ice chest if chloroform be added, and from it by dilution the standard solution is prepared.

In cerebrospinal fluids with a high protein content, smaller quantities are required for the test, in order that there may not be too much protein to read against the standard solution.

The authors give the following table of the protein level in normal and pathological fluids:

Normal	35–100	mg. per 100 c.c.
Active syphilis and tabes	100–200	,, ,, 100 ,,
Acute syphilis of the nervous system	200–600	,, ,, 100 ,,
Lethargic encephalitis	100–200	,, ,, 100 ,,
Recent cerebral vascular lesions	100–300	,, ,, 100 ,,
Tubercular meningitis	200–1000	,, ,, 100 ,,
Acute meningitis	400–1300	,, ,, 100 ,,
Xanthochromia with massive coagulation	2000	,, ,, 100 ,,

F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Barber, M. A. **Use of the single cell method in obtaining pure cultures of anaerobes.** *J. Exper. M.*, 1920, **32**, 295.

In this research the author has employed his well-known technical method for isolating single bacteria and has applied it to the study of anaerobic bacteria, and the production of pure cultures. He finds that cultivation from single spores gives a higher percentage of positive results than when single bacteria are employed. Boiling the medium before inoculation affords a sufficient degree of anaerobiosis for starting colonies from single spores. Exposure to air during the process of isolation has apparently no influence on the viability of spores of anaerobes although young bacilli suffer from a comparatively short exposure to free oxygen.

W. B.

Hetsch, H., u. **Schlossberger, H.** Biologische Eigenschaften der bei Wunddiphtherie gefundenen Diphtheriebazillen. [**Biological qualities of the diphtheria bacilli found in wound diphtheria.**] *München. med. Wchnschr.*, 1920, **67**, 1311.

This paper deals with the examination of 15 cultures of diphtheria-like bacilli isolated from wounds. Fourteen of these were proved to be true diphtheria bacilli, as was shown by the pathogenic action on guinea-pigs and mice inoculated by the percutaneous method of Kolle and Schlossberger. Further, these strains produced toxin the lethal action of which was neutralized by diphtheria antitoxin. By subcutaneous inoculation the lethal dose of culture varied between $\frac{1}{20}$ and $\frac{1}{1000}$ of a loopful for guinea-pigs and $\frac{1}{2}$ to $\frac{1}{100}$ of a loopful for mice. One of the fifteen cultures was atoxic and non-virulent, although in other respects it resembled true diphtheria bacilli. W. B.

Blake, F. G., and **Cecil, R. L.** **Studies on experimental pneumonia. VIII. Experimental *Streptococcus haemolyticus* pneumonia in monkeys.** *J. Exper. M.*, 1920, **32**, 401.

Attention has already been directed to the extensive researches of Blake and Cecil on experimental pneumonia (*Medical Science*, 1920, **3**, 63, 358). It was shown that, by intratracheal injection, typical pneumonia can be set up in monkeys. In the present, their eighth, paper they describe similar experiments which have been made with *Streptococcus haemolyticus*, the strain of microbe used having been isolated *post mortem* from a case of broncho-pneumonia in man. By passage through mice the virulence of the organism was exalted so that 0·00000001 c.c. was the lethal dose. The amount of broth culture employed for the intratracheal injection varied from 0·1 to 10·0 c.c. When quantities larger than 1·0 c.c. had to be used the streptococci were thrown down by the centrifuge and resuspended in portions of the supernatant broth, so that the required volume of culture did not exceed 1 c.c. Pneumonia ensued on intratracheal injection in nine normal monkeys, the lesions and symptoms being exactly comparable to those observed in man. Two pathological types of lesion were encountered, viz. interstitial pneumonia and confluent lobular pneumonia. The type of lesion seemed to bear some relation to the dose of culture injected, the interstitial type, apparently an indication of resistance, following the smaller doses. The distribution of the cocci in the lungs and the sites of early lesions showed that the microbes may invade the pulmonary tissue by penetrating the walls of the larger bronchi and that they are then carried by way of the interstitial framework of the lungs and its lymphatics. A previous injury to the respiratory surface by exposure to chlorine gas or a lowering of resistance by previous intraperitoneal injection of virulent *B. influenzae* greatly facilitated the invasion of the lung by *S. haemolyticus*. Ten excellent plates with nineteen figures complete this interesting research. W. B.

Thjøtta, Th., and **Eide, Odd Kinck.** **A mutating, mucoid paratyphoid bacillus isolated from the urine of a carrier.** *J. Bact.*, 1920, **5**, 501.

Attention was directed in *Medical Science* (1920, **2**, 278) to investigations by W. Fletcher on certain capsulated mucoid forms of paratyphoid bacilli which he had obtained from the stool of a carrier. The present authors have observed the sudden appearance of similar colonies in the urine of a patient suffering from cysto-pyelitis. This individual contracted paratyphoid fever of an ordinary type in December 1918, and in the following month had a severe attack of pyelitis of paratyphoid origin. This first attack was succeeded by numerous others until a condition of chronic pyelitis was induced with a constant discharge of paratyphoid bacilli in the urine. Until the month of May the strain of *B. paratyphosus* behaved normally in its reactions. At that time, however, a new type of colony, distinguished by its large size, its shiny wet aspect, and its inagglutinability, dominated in the plate cultures, and continued so till March 1920. In carbohydrate-containing media the atypical bacteria gave the fermentations of *B. paratyphosus.* As a rule the motility was slight or absent altogether, and in stained preparations the individual bacilli were exceedingly small and often arranged like diplococci. Emulsion of a colony in homologous serum produced no agglutination, although it was later shown that the agglutinability was specific although the maximum was only reached in a much longer time than when typical bacteria were employed in the test. Absorption of complement took place in exactly the same doses and time as in tests with typical strains. The atypical strains showed a marked capsule formation not unlike *B. pneumoniae,* Friedländer, which it also resembled in culture. Indeed, a strain of Friedländer's bacillus which the authors isolated from pneumonia in a guinea-pig could scarcely be distinguished in appearance from the atypical paratyphoid bacilli. The authors consider the atypical paratyphoid bacilli to be an instance of bacteria transmutation, the alteration being suddenly acquired and apparently breeding true. The new strain was also found to be pathogenic for mice, as was the original culture. Bactericidal tests with active human serum did not lend colour to the view that the atypical mucoid races were more resistant than typical bacilli. The observations of Fletcher and of the present authors afford evidence that bacterial 'transmutations' may occur both in the alimentary and in the uro-genital tract. W. B.

Gál, F. Experimentelle Studien über die Rolle des *Bacillus coli* und dessen Produkte bei künstlicher Peritonitis. [**Experimental studies on the part played by *Bacillus coli* and its products in artificially produced peritonitis.**] *Wien. klin. Wchnschr.*, 1920, **33**, 878.

The fact that many abdominal operations necessarily lead to contamination of the peritoneum with faecal matter containing in particular *Bacillus coli* which nevertheless may not give rise to any serious effects led the author to study the problem experimentally on guinea-pigs. An ordinary culture of *B. coli* was isolated from the normal human faeces and was used throughout the experiments. Filtrates, centrifuged extracts, and especially autolysed cultures were employed, the latter being obtained by suspending cultures in salt solution at 37° C. for 3 days. The author found that an autolysate of cultures of *B. coli* injected with a fatal dose of such organisms as *B. typhosus* or staphylococcus prevented a fatal issue although it had no influence on the opsonic index or on the bactericidal action of the serum. The autolysate caused a leucocytosis and marked phagocytosis of different bacteria injected into the peritoneal cavity, the bacteria being thus deprived of their toxicity. The chief site of the antibacterial conflict is in the great omentum. W. B.

Reina, G. Un caso di setticopiemia tubercolare. [**A case of tuberculous septicopyaemia.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 39.

Clinically the form had all the characteristics of an ordinary case of septicopyaemia consequent on a large abscess of the sacral and gluteal regions, in which many streptococci and staphylococci had been found. At the P.M. many abscesses were found in the cerebellum, lungs, kidney, and spleen, but at the bacteriological examination of these abscesses no pyogenic bacteria but enormous quantities of tubercle bacilli were found. This led to a thorough histopathological investigation of the various organs and to the consequent observation of a great number of tubercles so minute that they certainly could not have been seen by the naked eye. The author is of the opinion that, in this rare case of tuberculous septicopyaemia, the rapid and conspicuous spreading into all the organs of Koch's bacilli must have been influenced by the primary pyogenic abscess occurring in an heredo-tuberculous subject. C. d. F.

Schlossberger, H., u. Pfannenstiel, W. Tuberkulose Studien. I. Ueber die Differenzierung säurefester Bakterien. [**Studies in Tuberculosis. I. On the differentiation of acid-fast bacteria.**] *Deutsche med. Wchnschr.*, 1920, **46**, 1213.

This is a contribution to the much discussed question of the possibility of differentiating pathogenic tubercle bacilli from other acid-fast bacilli. The authors experimented with 16 genuine tubercle strains and 18 other acid-fast bacteria, some of which were pathogenic. They found that there are no morphological or tinctorial tests by which the two groups can with certainty be differentiated. Neither can they be separated by means of serum or acid agglutination tests. The differentiation by fermentation tests is also equivocal. The optimum temperature for growth seems, however, a more certain test for the differentiation. Apart from a race isolated by Arloing, true tubercle bacilli do not grow above 42° C., whereas, with the exception of an acid-fast organism called the 'trumpet' bacillus, all acid-fast tubercle-like bacilli from grass, butter, &c., grow at 50° C. or even higher. The tubercle bacilli of cold-blooded animals do not grow at 37° C. As Friedmann's so-called tortoise bacillus grows readily at this temperature, the authors consider that it should not be classed among the tubercle bacilli of cold-blooded animals. [Note. The 'trumpet' bacillus is an organism which was found on trumpets and many other musical instruments by Jacobitz and Kayser in 1910 (*München. med. Wchnschr.*, 1910, **57**, 1175).] W. B.

Goris, A. Composition chimique du bacille tuberculeux. [**The chemical composition of tubercle bacillus.**] *Ann. de l'Inst. Pasteur*, 1920, **34**, 497.

This is an elaborate investigation to determine the chemical composition of tubercle bacilli, and it confirms in the main the results of previous workers as detailed in the voluminous bibliography appended. By extraction with chloroform and subsequent digestion with alcohol and with water the author separated three types of substances. With respect to the fatty and waxy ingredients he refers particularly to a new substance, 'hyalinol,' which receives its name from its transparent appearance. He also obtained a waxy mixture which on saponification yielded two alcohols, the one, 'mykol,' melting at 65° C., the other, unnamed, with a melting-point of 100° C. Another substance obtained was laurate of mykol. Glycerides of oleic, palmitic, stearic, and arachidic acids were also noted as well as traces of caproic and butyric acids. The ash, from tubercle bacilli, which amounted to 2·5 per cent., was composed chiefly of phosphates and sulphates of sodium, potassium, calcium, and magnesium. The author agrees with previous observers that the substance which gives the characteristic acid-fast reaction is particularly the wax, and especially the acid derived therefrom by saponification—a view first clearly stated by Bulloch and Macleod in 1904.

W. B.

Medalia, L. S. 'Colour standards' for the colorimetric measurement of H-ion concentration P_H 1·2 to P_H 9·8. *J. Bact.*, 1920, **5**, 441.

This research was undertaken to make the standardization of culture media, according to H-ion concentration, adaptable to the means of an average laboratory. The fallacies of the titration method with phenolphthalein are pointed out. The author next explains the P_H nomenclature, and the electrolytic and colorimetric methods of estimating the H-ion concentration. He devises a method of obtaining the indicators in sterile solutions so that they can be kept indefinitely and used for testing acid formation by bacteria in cultures. Two-tenths per cent. alcoholic solutions of the indicators were prepared as 'stock solutions', kept in amber-coloured bottles, well stoppered with rubber stoppers and paraffined. From these were prepared watery solutions of strength 0·02 per cent. The indicators used were brom-phenol blue, methyl red, brom-cresol purple, brom-thymol blue, phenol red, cresol red, and thymol blue. The 'colour standards' chosen were brom-thymol blue (P_H 6·2 to P_H 7·8) and phenol red (P_H 6·8 to P_H 8·4). These were made up in the usual manner by superimposing the extreme colours of the particular indicator, seven pairs of tubes being used. This gives an interval of P_H 0·2 between each, the P_H of the first pair being 0·2 more alkaline than the initial range of the particular indicator. Phenol red does not make so clear cut a range at P_H 0·2 intervals as does brom-thymol blue. The P_H values were all calibrated with solutions of known hydrogen-ion concentration. A 'comparator block' is devised whereby culture media may be titrated till their reaction is that of the P_H selected. The arrangement is such that a simple factor is used to show how much normal NaOH or HCl must be added to neutralize 1 litre of the medium.

A wider range is necessary to measure the acid and alkali production by bacteria than that used for the standardization of culture media. The indicators used give a range P_H 1·4 to P_H 9·6, which is amply sufficient. The method for the preparation of colour standards from all the various indicators used was similar to those above described. It is found that these standards will keep well for over three months. They should be checked by setting up fresh sets monthly.

Further tests were undertaken to ascertain the ability of the various indicators to stand heating while being sterilized. Methyl red was the only one which decolorized on sterilization (in glucose and lactose bouillon). The action produced upon indicators by bacteria was also investigated. Again it was found that methyl red was the only one of the whole group that was decolorized. The organism used was a pure culture of *B. coli.*

By comparison with suitable standard colours the degree of acid or alkali production by bacteria could be carried out. The reading is simply a matter of matching colours, and the actual acid or alkali production by any given organism can easily be tested, hourly if desired, without disturbing the culture in any way, except in the case of methyl red, where fresh cultures are necessary for each reading.

In the third part of this paper the author proceeds to apply the above methods for measuring the H-ion concentration of other fluids and solutions such as urine, serum, &c. He concludes, with the remark, 'The practical application of the "colour standards" for the titration of culture media, by the H-ion concentration method, also for the P_H measurement of the acid or alkali production by bacteria, and for the P_H measurement of other fluids as described in this paper, is simple and easily handled, and because of its simplicity it promises to take a foremost place in the colorimetric measure- of the H-ion concentration of any fluid, as well as in bacteriology.'

W. A. M. S.

Meacham, M. R., Hopfield, J. H., and Acree, S. F. Preliminary note on the use of some mixed buffer materials for regulating the hydrogen-ion concentrations of culture media and of standard buffer solutions. *J. Bact.*, 1920, **5**, 491.

The authors desire to point out the advantages to be derived by using a single solution of two or three acids for giving a smooth curve relation between the H-ion concentrations 10^{-1} to 10^{-14} and the amount of alkali added to such mixture of acids. Since the range of acidity in biological work lies between P_H 3·0 to P_H 9·0, it is desirable to use such a buffer mixture. Also it is just in this region we find the largest change in P_H and therefore the largest errors when acid or alkali is added to the usual unbuffered culture media. For example, an error of only 0·2 c.c. N/1 alkali in 100 c.c. of corn-meal extract changes the P_H from 4 to 10. If the medium contains a mixture of buffer acids giving a smooth titration curve, any desired acidity of the medium can be produced and maintained with small experimental errors. The mixture of asparaginic acid and orthophosphoric acid used by Pieper in his synthetic medium gives nearly a straight line for the H-ion concentrations when the equi-molecular mixture of acids is treated with successive portions of alkali up to 5 molecules. This practically straight line is formed because a region of sharp inflection in the phosphoric acid titration curve, for example, is straightened out by adding another acid (or base), which when 65 to 85 per cent. neutralized gives a H-ion concentration approximating that of the point of inflexion in the phosphate inflexion curve. Slight deviations from a straight line also depend upon the buffer properties of other materials present, such as Witte's peptone, extracts of nutrient substances, and the acid or basic products formed by the fungi.

From their work and that of Prideaux, the authors believe that one solution containing asparaginic acid and ortho- (or pyro-) phosphoric acid in equimolecular quantities suffices to cover the entire range between 10^{-1} and 10^{-13} in practically a straight line relation between the H-ion concentrations and the number of molecules of alkali added to the mixture of the two acids. The buffer or culture solutions can be prepared and kept sterile by making the original solutions decidedly alkaline at ordinary temperatures instead of in the autoclave and afterwards adding a sterile strong acid in known amounts to secure solutions having higher H-ion concentrations. This one solution of the phosphoric and asparaginic acids can be made to give any desired H-ion concentration by simply adding varying known quantities of alkali and water to keep the solutions standard.

W. A. M. S.

Gorke, H. Auftreten von aplastischer Anämie nach Salvarsan. [**The occurrence of aplastic anaemia after salvarsan.**] *München. med. Wchnschr.*, 1920, **67**, 1226.

This is a record of two cases of aplastic anaemia or aleukia haemorrhagica, which appear to have been produced as the result of salvarsan injections. The first case was that of a woman aged 45 who, between June and August 1918, received 3 grm. of mercury in the form of *oleum cinereum* and 2·85 grm. of sodium salvarsan or neosalvarsan. Shortly after, she developed diarrhoea, stomatitis and great asthenia, which was considered to be mercurial in character. As she recovered she was submitted to a second course of salvarsan only, a total of 2·85 grm. being injected. The last dose of salvarsan was given on February 21, 1919, and on March 13 she was admitted into the Klinik of Minkowski, in Breslau, with bleeding from the gums, petechiae, and other symptoms of a haemorrhagic diathesis. A blood examination on March 14 showed, in addition to a reduction of erythrocytes, a marked leucopenia and a profound diminution in the platelet count. The actual results obtained were: erythrocytes 1,600,000, haemoglobin 30 per cent., colour index 0·97, leucocytes 2,800, neutrophils 20 per cent., lymphocytes 75 per cent., eosinophils 1 per cent., monocytes 4 per cent., and platelets 22,000 per c.mm. Five days later the count showed a marked deterioration, for there were then only 900,000 reds, 600 leucocytes, and 10,000 platelets per c.mm. The haemoglobin was 13 per cent., the colour index 0·7. Neutrophils constituted only 12 per cent. whereas the lymphocytes totalled 87 per cent. Death took place the day following that on which the latter count was made.

In addition to profound anaemia, the autopsy revealed haemorrhages in the skin and endocardium, while the red marrow was yellowish red in colour and microscopically showed a marked diminution of erythroblasts and myelocytes. No megakaryocytes were found at all. A second and somewhat similar case ending in recovery was that of a girl aged 19 who received, between the middle of February and the 27th of March, ten injections of silversalvarsan of a total of 1·95 grm. No mercury was administered. Three days after the last salvarsan injection she developed fever with bleeding from the gums and a membrane (diphtheria) formed on the tonsil. Epistaxis and anaemia followed. A blood count on April 11 showed a count of 2,600 leucocytes per c.mm., and 38,000 platelets. The neutrophils were 50 per cent., the lymphocytes 42 per cent. Recovery, however, gradually took place. The author deals with the literature of aplastic anaemia and its relation to Roentgen rays and benzol. He believes it to be established that a similar lesion may be set up, although rarely, by arsenobenzol, especially in idiosyncratic persons, with what is called a 'lymphatic diathesis'.

W. B.

Hahn, R., u. Fahr, Th. Zur Frage der Salvarsanschädigung. [**On the question of injuries from salvarsan.**] *München. med. Wchnschr.*, 1920, **67**, 1222.

This paper deals with the clinical and pathological aspects of six fatalities, in the General Hospital in Hamburg, following the injection of neosalvarsan. These were the first in Hahn's experience of several thousands of injections. Two of the cases were attacked in February 1919, one in April, and three in November. Three deaths were found to be due to so-called encephalitis haemorrhagica, two to changes in the liver (acute yellow atrophy or fatty infiltration), and one succumbed to exfoliative dermatitis with consequent sepsis. Five of the six patients were females, and of the encephalitis cases two had received 1·35 grm. of neosalvarsan in 3 doses of 0·45 grm., the third receiving 4 doses of 0·45 grm., the doses being properly interspaced. All had also received mercurial treatment. Of the two cases who developed atrophy and degeneration of the liver one had received 3 doses of 0·45 grm. neosalvarsan, whereas the other had received only 2 such doses. The case of exfoliative dermatitis—a male—received only 1 dose of 0·45 grm. neosalvarsan, which produced the skin lesions at once. He was regarded as the subject of arsenical idiosyncrasy, as a previous single injection of neosalvarsan had produced a similar attack from which he had recovered with difficulty. One of the authors (Fahr) discusses the morbid anatomy of these cases and analyses some of the views which have been expressed by others as to the causation. He states that he has seen 12 cases of acute yellow atrophy of the liver in the last few years, viz. 1 case in 1915, 1 in 1916, 6 in 1918, and 4 in 1919, an experience which has been frequently reported in recent medical literature.

W. B.

Reymann, G. C. On the transfer of the so-called normal antibodies from mother to offspring. *J. Immunol.*, 1920, **5**, 227.

This paper details a series of observations on goats and kids to determine whether normal bacterio-agglutinins and haemagglutinins are transmitted from parents to offspring. The bacterio-agglutinins specially examined were those which act on *B. typhosus* and *B. coli*, while the haemagglutinins were those which clump the erythrocytes of the horse or the rabbit. Seven pairs of twins were the subject of examination. In only one of the fourteen animals did agglutinins occur, all the others being born without agglutinating properties in their sera, although such properties were present in the maternal sera. Agglutinins appear in the sera of kids later on and are apparently derived through the milk, in which they are found to accumulate at parturition. From the milk as well as from the kid's serum agglutinins disappear in a few days but are followed by a reappearance, probably in consequence of an immunization from the digestive tract. In order to determine the degree of transmission of agglutinin through the milk Ehrlich's classical 'changeling' experiment was undertaken in such a manner that one kid of a pair was removed from the mother before suckling and fed on boiled cows' milk, whereas the other was permitted to suckle. One of two such experiments indicated that the agglutinin was transmitted by mother's milk. In the other experiment the result was dubious. The agglutinins—absent at birth—may appear in the serum within 11 hours after birth. Injections of horse erythrocytes into kids increases the agglutinin for such erythrocytes, but also for *B. coli*, and *vice versa* the injection of *B. coli* evokes agglutinin production not only for the homologous bacillus but also for the red corpuscles of the horse. The experiments were carried out in the State Serum Institute in Copenhagen.

W. B.

Schmidt, C. L. A. The antigenic properties of haemocyanin. *J. Immunol.*, 1920, **5**, 259.

Haemocyanin is a copper-protein compound found in the circulating fluid of many crustacea, mollusca, and other invertebrates, and functionally it appears to behave as an oxygen carrier, although, unlike haemoglobin, it is not confined to any particular cells. Long ago (1903) von Dungern showed that it was possible to immunize rabbits against the circulating fluid of cephalopods, and he found copper in the specific precipitate obtained when the antibody was mixed with octopus serum. The present author experimented with haemocyanin obtained from the abalone (Haliotis), a mother-of-pearl shell-fish found on the Pacific Coast. Immunization experiments were carried out on four rabbits, and their sera were found to give precipitin and complement-fixation tests with solutions of haemocyanin. Although non-toxic, even in large doses, for normal guinea-pigs, typical anaphylactic shock was produced by the subsequent injection of a smaller dose.

W. B.

Gasbarrini, A. Ulteriore contributo allo studio di una particolare forma di emoglobinuria sperimentale. Su di un siero antiemoglobinurico. [**Further investigations on a special form of haemoglobinuria. On an antihaemoglobinuric serum.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 13.

The author had already shown some years ago that by means of intraperitoneal injections of a certain quantity of laked and isotonized blood it is possible to cause in dogs and rabbits a form of haemoglobinuria similar to the malarial and quinine haemoglobinuria of man. He has now made fresh investigations from which it results that it is possible to protect the animals experimented upon against the above-mentioned haemoglobinuria if, previously to the injection of the laked and isotonized blood, the animals are inoculated with a certain dose of inactivated serum obtained from animals made haemoglobinuric by the described means. From these facts the author is led to think that it is perhaps possible to prepare by his method an antihaemorrhagic serum useful for the cure of certain haemorrhagic diseases. Preliminary attempts made in cases of purpura haemorrhagica and of favism [1] were attended by encouraging results.

C. d. F.

Mazzei, A. Ricerche sulla irite anafilattica. [**Anaphylactic iritis.**] *Riforma med.*, 1920, **36**, 853.

Experimental investigations, the results of which are summarized by the author as follows: If a heterologous serum is injected into the anterior chamber of the eye of rabbits, after the iris has been a little lacerated, and the same serum is re-injected after a period of incubation, the iris shows a rather intense reaction which can be considered as a manifestation of local anaphylaxis. C. d. F.

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[1] Favism [fabism] is a condition repeatedly observed in Italy, and is believed to be due to poisoning by some product in beans (*Vicia faba*). In addition to nervous phenomena the signs of fabism include diminution in the number of red blood corpuscles, intense haemoglobinuria, and urobilinuria.

Schiassi, F. L'autoanafilassi a frigore nell' emoglobinuria parossistica. [**The autoanaphylaxis due to cold in paroxysmal haemoglobinuria.**] *Policlin.*, 1920, **27**, Sez. Med., 346–57.

Schiassi has confirmed many of the results of earlier writers on auto-anaphylaxis in paroxysmal haemoglobinuria and here lays stress chiefly on the part played by cold. He views anaphylaxis in terms of complement, antigen, &c., and does not yet adopt the more physical terminology of the French School. He therefore concludes that cold is an antigen (which almost strains the accepted meaning of words) and calls attention to the remarkable circumstance that a purely physical agent can act in this way. Whether cold, exercise, and other causes of the immediate attack in this disease are really antigens, or merely liberate them from some pre-existing complex, is well worth inquiry, and Schiassi contributes many careful and well recorded experiments. G. W.

Durand. Encefalite letargica. [**Lethargic encephalitis.**] *Riforma med.*, 1920, **36**, 789.

The bacterioscopic and ultra-microscopic examinations of blood and cerebrospinal fluid from cases of lethargic encephalitis were constantly attended by negative results. Subcutaneous and intravenous inoculations of blood and cerebrospinal fluid into rabbits, guinea-pigs, and white mice were also entirely unsuccessful. Culture from the cerebrospinal fluid remained sterile. Bouillon culture from the blood of four out of six different cases allowed the author to isolate a very small Gram-positive coccus, of which he describes the biological properties, without, however, considering it as the specific agent of the malady. This because, in severe disease of infectious origin, the blood may be invaded either by the specific germ localized before in a certain organ, or by other germs merely complicating the morbid process without being directly connected with its causation.
C. d. F.

Tron, G. L'encefalite letargica nei suoi rapporti colle infezioni miste. [**Lethargic encephalitis: its possible relation with mixed infections.**] *Gazz. d. osp.*, 1920, **41**, 788.

The author, after having briefly reviewed the opinion expressed by other investigators on the aetiology of encephalitis lethargica, puts forward the suggestion that its different clinical forms may be due to the presence in the tissues of various germs of different pathogenic power, perhaps associated with an as yet unknown specific virus. C. d. F.

Bastai, P. Sull' eziologia dell' encefalite letargica. [**On the aetiology of lethargic encephalitis.**] *Gazz. d. osp.*, 1920, **41**, 663.

Summary of a communication made at the 'Accademia Medico-Fisica di Firenze', April 1920. Seven rats were inoculated intraspinally with the filtered emulsion of three human brains from typical cases of lethargic encephalitis. The animals soon became affected by a disease chiefly characterized by lethargy, from which, however, they recovered in about 8 days. At the microscopic examination of the brains small perivascular haemorrhages and a moderate small-celled infiltration of the brain substance were found. The same facts were noticed in the walls of the cerebral ventricles, together with a more remarkable lymphocytosis of the cerebral spinal fluid. From cultures made from the filtered emulsions either of human or cat's brain a very small coccus was isolated. The author therefore is of the opinion that the specific agent of lethargic encephalitis may belong to the group of filter-passing cocci.

At the same meeting of the above-mentioned Academy, Pisani and Varisco made a communication regarding their isolation from other cases of encephalitis of a diplococcus different in certain respects from all known diplococci. In the opinion of the authors, however, their diplococcus is only a germ frequently associated with the still unknown specific agent of the disease. C. d. F.

Sala, G. Sopra un reperto isopatologico relativo al ganglio ciliare in casi di cosidetta 'encefalite letargica'. [**Histo-pathological observations on the ciliary ganglion in cases of lethargic encephalitis.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 93.

Investigations were made by Cajal's reduced silver method on the ciliary ganglion from cases of lethargic encephalitis which had presented during life various pupillary troubles. Some ganglion cells no longer showed their characteristic structure and appeared transformed into an irregular protoplasmic mass containing many small and roundish bodies stained black by the reduced silver. The author puts forward the suggestion that they may be granules of pigment but with characters somewhat different from those one finds in normal spinal and sympathetic ganglion-cells. Sala's observations remind one very much of the pigment-like granules described by Da Fano and Ingleby (*Proc. R. Soc. Med.* 1919, **12** (*Sect. of Path.*), 42), also in cases of lethargic encephalitis and in places of the central nervous system where brown or black pigment does not generally occur. C. d. F.

Monti, A., e **Tibaldi, E.** Sulla patologia e patogenesi dell' encefalite letargica. [**On the pathology and pathogenesis of lethargic encephalitis.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 97.

Investigations were extended to all organs of seven cases dead during the last Italian epidemic of the disease. The principal lesions observed were: congestion and minute haemorrhages of the brain, particularly noticeable in the pia mater, grey substance of cerebral cortex, lenticular nucleus, external capsule, mid-brain, pons, and medulla oblongata. At the microscopic examination of the same regions slight haemorrhagic perivascular suffusions and small-celled infiltrations were seen. In these, sometimes plasma cells, sometimes 'granulous and pigmentiferous elements' (macrophages?) could be remarked. In the neighbourhood of such areas the nerve-cells showed various secondary lesions and, particularly in one case, 'necrotic and involution phenomena similar to those one meets with in small foci of thrombotic softening'. The endothelium of many blood-vessels appeared beset with minute hyaline or granular clumps, and sometimes also with lipoid and fatty granules. Alterations of the same kind were found in the spinal cord, particularly at the level of the cervical enlargement and in the spinal ganglia, where a proliferation of the capsular endothelium was seen. In the muscles there appeared to be a remarkable proliferation of the nuclei of the sarcolemma and other lesions similar to those described first by Golgi in cases of tetanus; a fact which very much favours the possible toxic nature of the malady. Other lesions were found in the lungs, pericardium, intestine, adrenals, liver and kidneys, particularly in the form of congestion with dilatation of the blood-vessels and haemorrhages. A remarkable degree of congestion and tumefaction of the Peyer's patches, of the solitary follicles of the intestine, and of the spleen were also frequently found.

All attempts to isolate bacteria from the central nervous system and to transmit the disease to rabbits, guinea-pigs, mice, and dogs were attended by negative results.

In the second part of their paper the authors point out that these lesions do not differ from those seen in severe cases of influenza, more particularly in its so-called nervous form. C. d. F.

Pirone, R. Sulla coltivabilità del virus rabbico. [**On the cultivation of virus hydrophobiae.**] *Riforma med.*, 1920, **36**, 782.

Investigations of an incomplete character which were made before the war with the purpose of controlling the results arrived at by Noguchi. The author was unable subsequently to repeat and complete his experiments, but he thought it useful to publish them without further delay as they confirm the possibility of cultivating the virus of hydrophobia by Noguchi's method. In the cultures of two different series of experiments bodies similar to those described by J. Koch were found. C. d. F.

Mallory, F. B., and **Medlar, E. M. The skin lesions in measles.** *J. Med. Research*, 1920, **41**, 327.

This paper records a research, extending over two years, into the cause of measles. Various cocci and a bacillus have been described by investigators and recently Tunnicliff has grown a Gram-positive coccus from the blood of many cases.

The authors hold that the cutaneous rash and Koplik's spots must be due to the causal agent of the disease, and emphasize the importance of the study of these lesions; the respiratory tract and conjunctiva are more liable to harbour secondary invaders.

Besides bacterial examination of the latter sites and the blood in the pre-eruptive and early post-eruptive periods, portions of skin containing the rash were excised from 35 patients during life, and buccal mucous membrane with Koplik's spots from six patients. The histological features of the cutaneous lesions are practically the same as those of Koplik's spots. They consist in a mitotic activity of the vascular endothelium of the corium, a perivascular infiltration by 'endothelial leucocytes', mitotic activity in these infiltrating leucocytes, and very sparse infiltration by other leucocytes; similar infiltration of hair-sheaths and sebaceous glands; oedema of epidermal cells; the formation of pustules, consisting of small collections of serum and endothelial leucocytes, between the cells of the epidermis.

Gram-positive bodies of varying size, usually about that of a very small coccus, were found in the vascular endothelium in the rash and buccal mucosa, as many as seven bodies to a cell. The authors think it probable that these bodies are fragments of cocci, possibly the causal agent. Investigation by inoculation of monkeys is advocated.

There are 19 microphotographic illustrations and one drawing of the coccal bodies in endothelial cells. W. W. W.

Berry, F. B. The regeneration of smooth muscle-cells. *J. Med. Research*, 1920, **41**, 365.

In the healing of defects in smooth muscle, the edges are bound together by scar tissue, and though mitotic and amitotic division of muscle-cells have been observed in the wounds, the consensus of opinion at present is that the muscle-cells play little part in the process of healing in the higher vertebrates.

The author of this paper found active young muscle-cells, showing mitotic figures, in the granulation tissue closing a curette injury in the myometrium made 4 days previously to hysterectomy.

He found a similar condition in the uterus of two rabbits and three guinea-pigs experimentally wounded at varying periods of from two to five days previous to removal, and also in the stomachs of two rabbits incised and sutured four and six days before removal.

In older wounds of these organs in the human body and in animals, he found the scar tissue partially resorbed and shrunken, with pulling together of the newly formed muscle fibres, so that location of the site of the wound was difficult.

Dr. Berry therefore considers that this amount of activity of the muscle fibres, though regarded by previous investigators as so insignificant as to be disregarded, is worthy of being called regeneration.

He emphasizes the importance of close approximation of the edges of wounds in smooth muscle tissue, in order to obtain a minimum of scar and a maximum of new muscle.

There are seven microphotographic illustrations. W. W. W.

Fischer, W., u. Birt, E. Ein Paraffingranulom des Penis. [**A paraffin granuloma of the penis.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1920, **66**, 494–500.

Clinical observation and histopathological examination of a peculiar case of granuloma of the penis. The 'tumour' had to be surgically removed and was found to consist of a series of more or less incomplete chambers filled with paraffin. The walls of the cavities were formed in part by thin septa of connective tissue and in part by the stretched cavernous tissue of the organ. Here and there a moderate small-celled infiltration and a few giant-cells were noticed. C. d. F.

Riquier, G. C. Intorno alla sistematizzazione fascicolare dei nervi periferici. [**On fascicular systematization of peripheral nerves.**] *Boll. d. Soc. med.-chir. di Pavia*, 1920, **33**, 9.

Investigations were made in order to control the result obtained by Dustin, who found that in the median, radial, and ulnar nerves of man, the nerve fasciculi divide and anastomose within the nerve-trunk so as to form a large and complicated plexus which makes a functional systematization on an anatomical basis impossible. But Riquier, having made serial sections of pieces of human cubital nerve, even as long as four centimetres, came to the conclusion that the fasciculi change in number and size according to the level at which the sections are made, but have fundamentally the same position along the nerve-trunk; some fasciculi even maintain a constant situation in the whole series. The author therefore thinks that an irregular mixing of nerve-bundles and fasciculi within the same nerve-trunk ought to be excluded. This, however, has little value from a functional point of view because the fasciculi, though maintaining a certain individuality along the nerve, may contain both sensory and motor nerve-fibres. The question can be resolved only by having recourse to experimental sections of spinal roots in high vertebrates, but particularly in monkeys. C. d. F.

Begtrup, E. Lidt om fedtlever. [**Concerning fatty liver.**] *Ugesk. f. Læger*, 1920, **82**, 1199–1204.

After giving a definition of fatty liver, Begtrup notes that it is commonly associated with prolonged indulgence in alcohol, and that it is generally regarded as a comparatively harmless condition, seldom proving fatal *per se*. He has collected the records of a series of necropsies made before and after April 1, 1917, when far-reaching restrictions on the sale of alcohol were introduced in Denmark. He chose at random the years 1910 and 1915, as well as the year April 1, 1916–April 1, 1917, as standards for comparison with the two following years. In 1910 there were 224 necropsies, among which there were 52 cases of undoubted, macroscopically demonstrable, fatty liver. This represented 23·2 per cent. of the total. The corresponding percentages for 1915 and the year ending April 1, 1917, were 15·5 and 18·1 per cent. In the two subsequent years the incidence of fatty liver among 193 and 177 necropsies was 6·2 and 4·5 per cent. respectively. There was no such abrupt fall in the incidence of cirrhosis of the liver since April 1, 1917. In 1910 this condition was found in 6 per cent. of all the necropsies, and in 1918 in 4·9 per cent. Begtrup concludes from these figures that while the incidence of fatty liver can speedily be reduced almost to a negligible quantity by withholding alcohol from the community for even a short period, cirrhosis of the liver is a permanent consequence of alcoholism, and the effect of prohibition is therefore not reflected in an immediate and abrupt fall in the frequency of cirrhosis of the liver in the dead house.

C. L.

Lenaz, L. Sulla patogenesi dei cosidetti itteri emolitici. [**The pathogenesis of so-called haemolytic icterus.**] *Policlin.*, 1920, **27**, Sez. Med., 337–45.

Lenaz concludes 'rather than a true disease, haemolytic icterus is an error of development, a condition of constitutional inferiority of the blood-making organs, characterized by an arrest of development and persistence of embryonic structure beyond the normal time'. The crucial test of this should include the examination of the erythrocytes of the newly born for those characteristics which are found in acholuric jaundice. Lenaz does not seem to have done this. G. W.

Fagiuoli, A. Contributo allo studio degli itteri emolitici secondari. [**A contribution to the study of secondary haemolytic jaundice.**] *Policlin.*, 1920, **27**, Sez. Med., 317–37.

Fagiuoli describes a case of acholuric jaundice associated with and perhaps dependent on tuberculosis. The patient was aged 17, and there was no family history of jaundice or splenomegaly, although there was a history of tuberculosis in the father. The case is important inasmuch as it came to autopsy. Although there are many reports on the spleen of such cases there are still so few complete autopsy reports as to make this one of considerable value.

The liver showed complete absence of cirrhotic changes and of cellular infiltration. The central veins of the lobules and the interlobular veins were congested. The periphery of the lobules showed some tendency to fatty changes, the centres were well preserved. There was a great increase of Kupffer cells, and these contained many included erythrocytes (4–6 or more). The hepatic cells towards the centre of the lobules showed abundant iron-containing pigment in very small granules. The spleen exhibited considerable activity of macrophages shown by included red cells. These were in the pulp alone. Neither the sinuses nor germ centres showed any cell inclusions. Fine ferruginous pigment was found everywhere except in the follicles. The kidneys contained fine pigment in the epithelium of the contorted convoluted tubules and also free in the tubules of the loops of Henle, some of which were blocked up. Both the bone-marrow and glands showed evidence of erythrophagocytosis.

There was advanced tuberculosis of the lungs and of lymphatic glands.

A second case, also tuberculous in origin, gave similar but less evident findings. G. W.

Mallory, F. B. The type cell of the so-called dural endothelioma. *J. Med. Research*, 1920, **41**, 349.

Dr. Mallory here gives the results of an investigation of the histology of thirty examples of this tumour. He concludes that it does not arise from the cells of the dura, but from the cells of the arachnoid that have budded into the dura to form the Pacchionian bodies or arachnoid villi. Further, the arachnoid cells that give rise to the tumour are not endothelial but fibroblastic. He therefore claims that the tumour should be named 'arachnoid fibroblastoma'. The statement that 'there is no dural endothelium' is supported in this paper only by the fact that the development in the embryo of the intradural space is later than the development of the vessels. So the opposed surfaces of dura and arachnoid, including arachnoid villi, are covered by fibroblasts. Also, 'the numerous spaces in the villi, probably for the passage of lymph, are lined by fibroblasts'. Arachnoid villi are developed by the ingrowth of arachnoid cells into the dura. Normally, the dural cells in the vicinity of the ingrowing villi are stimulated to form more elastic fibre than elsewhere. From the fact that in the intradural part of the tumour the whorls contain more collagen and elastin than in other parts of the tumour, Dr. Mallory concludes that the fibres that are in excess are produced by the dural cells. This stimulation of the dural cells by the tumour points to a similarity in growth between the tumour and the arachnoid villi.

The other argument given in favour of the tumour cell in question being a fibroblast rather than an endothelial cell is that it forms collagen. Dr. Mallory goes on to point out a resemblance between the meningeal tumour and the tumours known by the various names of neurofibroma, false neuroma, fibroma molluscum, plexiform neurofibroma, von Recklinghausen's disease. He holds that all these tumours arise from the fibroblasts of the perineurium. These cells differ from those of the epi- and endo-neurium. He considers that the perineurium is probably not an extension of arachnoid, but is an analogous differentiation of the mesenchyma round the nerves. These perineurial tumours sometimes have an oedematous, myxomatoid structure, but sometimes the cells and collagen fibres are clumped in masses, with a palisade appearance similar to that seen in the meningeal tumour, as well as in other tumours such as the uterine leiomyoma. These tumours invade the nerve-tissue and sometimes extend along it to such a degree as to cause the so-called plexiform neurofibroma. In this respect they differ from the meningeal tumour, which, though arising from arachnoid cells, never invades the arachnoid, and so does not invade the brain. Dr. Mallory would have all these tumours named perineurial fibroblastoma. He would give the same title to the tumours of the nervus acusticus and central nerves, pointing out that the neuroglia and nerve-fibres they sometimes contain belong to the invaded nerve.

There are twenty microphotographic illustrations.

W. W. W.

BIOCHEMISTRY

Weiss, M. Colorimetrische Phenolbestimmung im Harn. [**The estimation of phenol in urine.**] *Biochem. Ztschr.*, 1920, **110**, 258.

By treating diluted urine with an acid solution of mercuric sulphate for 15 minutes and adding sodium nitrate, all the combined and free phenols react to give the Millon red colour. This can be compared with a standard solution of tyrosin treated with the acid sulphate. Diarrhoea and constipation influence the normal values for phenol. Weiss finds up to four times the normal value for phenol in cases of carcinoma and tuberculosis of the intestinal tract. He believes the estimation may be of value in differential diagnosis of difficult cases. C. G. L. W.

Myers, V. C., and **Short, J. J.** **Estimation of chlorides in blood.** *J. Biol. Chem.*, 1920, **44**, 47.

The authors describe a method of chloride estimation in blood, involving the use of the same blood and filtrate used for the estimation of sugar.

R. A. P.

Bell, R. D., and **Doisy, E. A.** **Phosphorus.** *J. Biol. Chem.* 1920, **44**, 55.

New rapid methods (colorimetric) are described for the determination of inorganic, organic, and total phosphorus in urine; also of inorganic and acid soluble phosphorus in blood. R. A. P.

Denis, W., and **Aldrich, M.** **Note on the preservation of specimens of blood intended for sugar determinations.** *J. Biol. Chem.*, 1920, **44**, 203.

The addition of 1 drop of commercial formalin (40 per cent.) to 5 c.c. of oxalated blood enables a blood specimen to be kept for 96 hours before analysis of the sugar content. The formaldehyde in practice does not interfere with the Folin-Wu sugar determination. R. A. P.

Engleson, H. Über die Bestimmung kleinster Arsenmengen im Harn, Blut und anderen Körperflüssigkeiten nebst der Arsenbilanz bei Silbersalvarsanbehandlung. [**The estimation of minimal quantities of arsenic in body fluids. The arsenic balance in silversalvarsan treatment.**] *Ztschr. f. physiol. Chem.*, 1920, **111**, 201.

The reaction $3\,As_2O_3 + 2\,HBrO_3 = 3\,As_2O_5 + 2\,HBr$ is used. The end of the reaction can be ascertained by adding an indicator such as methyl orange or indigo, which is decolorized by an excess of bromic acid. The details of the analysis must be seen in the original article, amounts of arsenic smaller than 0·05 mg. are estimated with accuracy. An interesting table showing the partition of arsenic in blood and urine after silversalvarsan treatment is given. When 292·5 mg. of arsenic in this form were given 26·6 per cent. was excreted in the urine. The major part of the arsenic was retained in the body sixteen days after the last injection. The amount of arsenic in 5 c.c. of blood during the treatment varied between 0·035 mg. and 0·002 mg. C. G. L. W.

Fürth, O., u. **Nobel, E.** Colorimetrische Untersuchungen über das Tryptophan. [**Colorimetric experiments on tryptophane.**] *Biochem. Ztschr.*, 1920, **109**, 103.

The authors have employed a colorimetric method (Voisenet) for the estimation of the amino-acid tryptophane. They have obtained some interesting figures, of which a few may be quoted. Normal horse serum has a tryptophane content of 0·2–0·4 per cent. The albumin fraction of such serum contains 1·2 per cent., and the globulin 4·1–4·7 per cent. Other globulins contain 4·6–6·1 per cent. tryptophane. Casein contains 2 per cent. The tryptophane content of protein from human milk, interestingly enough, is more than that of cow's milk, though the protein content is less.

Haemoglobin is tryptophane-free. Egg albumen, edestin, and muscle proteins contain 2–3½ per cent. Keratin is tryptophane-free; gelatin, elastin, and fibrin are tryptophane-free. The liver, spleen, and thyroid are rich in tryptophane, the brain free from it. Tryptophane content of an individual of 58½ kg. would be 115 grm.

By tryptic digestion of fibrin, it is not possible to split off more than ⅔ of the existent tryptophane in the free form. So far as light is shed on the position of tryptophane in the protein molecule, it seems that it must be distributed evenly throughout it. In digestion of protein, the appearance of tryptophane runs parallel to the appearance of amino-acids. It is interesting in connexion with these experiments to remember that thyroidin has been shown to be a tryptophane compound, and points to the general importance to life of the amino-acid originally discovered by Hopkins and Cole. R. A. P.

Rusznyák, S. Physikalisch-chemische Untersuchungen an Körperflüssigkeiten. Der Zustand des Chlors im Serum und Plasma. [**The physical chemistry of body fluids. I. Chlorine in serum and plasma.**] *Biochem. Ztschr.*, 1920, **110**, 60.

The chlorine content of hirudin plasma and serum was determined before and after filtration through a collodion membrane. In this way any chlorine held in colloidal combination should be retained by the filter. Experiments were carried out with blood from various pathological conditions. The chlorine content of the filtrate was the same as that of the original fluid; there is therefore no chlorine combined with colloids in the blood. C. G. L. W.

Atzler, E., u. Döhring, E. Physikalisch-chemische Beiträge zum Problem der Blutgerinnung. [**The physical chemistry of blood clotting.**] *Biochem. Ztschr.*, 1920, **110**, 245.

In an attempt to ascertain whether the clotting of the blood was a chemical change accompanied by the evolution of heat, measurements were made using apparatus capable of detecting very small amounts. They were unable to detect any heat exchange. No change in volume or in electrical conductivity was found when clotting took place.

C. G. L. W.

Neubauer, E. Beiträge zur Kenntnis der Gallensekretion. [**Contributions to our knowledge of the secretion of bile.**] *Biochem. Ztschr.*, 1920, **109**, 83.

A number of cases of cholelithiasis show symptoms attributed to the autonomic sympathetic systems. The author has studied the behaviour of the bile in normal rabbits with fistulae. He has further tried the effect of injecting several substances such as pilocarpin, atropin, and adrenalin. Pilocarpin caused a slight concentration of the bile. Atropin had no effect. Adrenalin (which stimulates sympathetic factors) caused a decrease in the amount of bile excreted, with increase of specific gravity and of dried extract. When injected subcutaneously, adrenalin caused a production of sugar in the bile, sugar being normally absent from it.

R. A. P.

Forssman, J. Ein neues Krankheitsbild nach Seruminjektionen. [**A new symptom-complex after injections of serum.**] *Biochem. Ztschr.*, 1920, **110**, 164.

In another paper reviewed in this number Forssman has reported the results of the direct injection of immune sera into the arterial system. In this paper he reports a most unusual symptom-complex resulting from the injection of sera centrally into the aorta.

If very small quantities of sheep's haemolytic serum from rabbits are injected in this way—amounts much smaller than are necessary to produce anaphylaxis—the animals are seized with disturbance of equilibration, so that they only progress in a circle; the feet may be poised in the air and the animal perform rolling movements which persist for a long time. There are ocular disturbances, exophthalmos, with sometimes hemianopsia. There are none of the symptoms which are commonly regarded as anaphylactic. The reaction is specific, for neither normal rabbit nor normal sheep's serum produce this effect, also high titre immune rabbit's serum and one which contains heterologous sheep's haemolysin. Ordinary sheep's haemolytic sera and sheep's haemolytic serum produced by the injection of guinea-pig organs give the reaction regularly.

The ordinary anaphylactic phenomena were not influenced by the mode of injection.

The substance which provokes the symptoms described above is a new immune body, and is not the same as that causing anaphylactic death. The action of the substance is on the cerebellum owing to the anatomical arrangement of the large arterial vessel. The substance reaches this organ in greater concentration through the right vertebral artery when it is injected towards the heart than when the serum is injected into the carotid peripherally.

In order to ascertain whether the mixture of blood with the serum produced the body, experiments were made by injecting mixtures. In some cases disturbance of equilibrium and death of the animal occurred, but no strabismus. Adrenalin and thyroidin were also tried, but no difference was found whether the serum was injected centrally or peripherally. In the case of adrenalin, it was found that this substance increased the toxicity of the serum in amounts which would have caused no effect either from the serum or from the drug. C. G. L. W.

Benedict, F. G. The basal metabolism of boys from one to thirteen years of age. *Proc. Nat. Acad. Sc.*, 1920, **6**, 7. (*Chem. Abstr.*, 1920, **14**, 3450.)

A curve is presented showing calories of basal metabolism to body-weight arrived at by a study of 128 boys, which shows such close concordance that it can be used to predict the probable basal metabolism of boys within this period. C. G. L. W.

Sherman, H. C. Calcium requirement of maintenance in man. *J. Biol. Chem.*, 1920, **44**, 21.

Experiments on animals by Osborne and Mendel have shown the importance of calcium in the diet. Further, McCollum, Simmonds, and Parsons have shown that calcium is a limiting factor in many of our staple foods. In this paper the author has collected the results of some 97 experiments upon the calcium requirement of man. The average needed appears to be 0·45 grm. per diem, an amount which the author considers is not at all overestimated. Food should contain about 1·0 grm. of calcium to every 100 grm. of protein. Out of several dietary studies it was shown that 1 in 6 was below the estimated need in calcium. The supplementing of the diet with calcium rich foods such as milk is recommended as being preferable to adding calcium carbonate or phosphate to other foods. R. A. P.

Rona, E. Über die Wirksamkeit der Fermente unter abnormen Bedingungen und über die angebliche Aldehydnatur der Enzyme. [**On the action of ferments under abnormal conditions and the supposed aldehyde nature of the enzyme.**] *Biochem. Ztschr.*, 1920, **109**, 279.

The theory of the aldehyde nature of fermentation is not confirmed by the experiments of the paper. In the presence of reagents which react with aldehydes—such as sodium bisulphite, pepsin, trypsin, amylase, emulsin—invertase and maltase showed no, or practically no, decreased action.

R. A. P.

Forssman, J. Der Ursprung des anaphylaktischen Schockes. [**The cause of anaphylactic shock.**] *Biochem. Ztschr.*, 1920, **110**, 132.

The cause of anaphylactic shock is still unknown. It has been assumed that the lungs play a predominant rôle, but even so it has been debated whether the pulmonary symptoms are of peripheral or central origin. Little also is known concerning the spasms and sudden fall in body temperature. These have been supposed to be cerebral in origin, but here also no real information is available as to the primary or secondary character of the cerebral disturbance, as little is known regarding the function of the liver in anaphylactic shock. Forssman has investigated the anaphylactic shock produced by injecting sheep's haemolytic serum into guinea-pigs. He believes that the antibody is specifically combined with guinea-pig organs. Anti-anaphylaxis ensues when the animal is treated with a sublethal dose of the serum. There is a radical difference between ordinary anaphylaxis and the 'reversed' condition. In the former nearly all the antibody is combined with the antigen. In the second condition it is known that guinea-pig organs contain a large amount of antigen, far more than is necessary to combine with the antibody. The process of anti-anaphylaxis must therefore be different from that occurring in the ordinary process. Forssman explains this by assuming varying degrees of avidity in the antigens. The one antigen is that which reacts with about two lethal doses of the antibody, while the second reacts by lower antibody concentration. This latter forms the smaller fraction of the total. Forssman has attempted to ascertain whether the antigen which produces acute shock is present in all organs, or is mainly confined to certain of them. In order to test this, sera were injected partly into the substance of organs themselves and partly into the main vessels of the organs. The results were compared with the effect of similar amounts injected by the usual intravenous route. In none of the cases was it possible to induce lethal anaphylactic shock by injection into the organs. From this it is concluded that the antibody can only be effective by acting on the vessels.

Narcosis partially inhibits anaphylaxis only when the serum injection takes place shortly after the administration of the drug. If several hours elapse, the narcosis has no effect.

In a series of experiments, extirpations of the kidneys, spleen, intestines, liver, and suprarenals were carried out. The animals were then treated intravenously with the dose of serum which would cause death in the intact animal. In the case of the kidneys, it appears that double nephrectomy produces a total resistance to the lethal dose. This is due to the retention in the organism of secretion products which are otherwise eliminated. Intestine and spleen have no influence on shock. The liver does not contain the antigen which provokes shock. The experiments point further to the notion that the toxic effect of the serum is inhibited by the presence of the liver. There was indirect evidence that the adrenals did not influence shock. The brain likewise does not participate as a primary cause in shock. By passage through this organ the serum is partly detoxicated, as is the case with the liver. By injection of serum deep into the aorta, between the third and fourth ribs, no shock is obtained by a lethal dose. By injection into the left ventricle shock occurred in the same way as if it were injected into the vena jugularis.

It would therefore appear that the vascular region which is of importance in shock is the coronary arteries or the bronchial arteries. It is uncertain whether one or both of these areas is responsible.

C. G. L. W.

Underhill, F. P., and Simpson, G. E. The effect of diet on the excretion of indican and the phenols. *J. Biol. Chem.*, 1920, **44**, 69.

With the object of gaining first information upon what diets favour or diminish intestinal putrefaction, the authors have studied the indican and phenol excretion in three normal individuals and in a dog. Phenol and indican represent substances produced by intestinal putrefaction, and are made more or less harmless by conjugation with sulphate on their passage through the body, prior to excretion in the urine. The authors found that, if disturbing factors in the experiments, such as constipation, were eliminated, diets containing large amounts of protein favoured the excretion of these putrefactive substances. Herter and Kendall and others have previously shown that protein diets favour growth of putrefactive bacteria in the intestine. On the other hand, a diet containing a large amount of lactose lowers the formation of indican and phenol. Such a diet has been shown to promote the growth of acidophile bacteria by Hall and Rettger. The correlation between the two sets of observations seems to hold well, and points the way to the regulation of intestinal putrefaction by careful dieting.

R. A. P.

Goldberger, J., Wheeler, A. G., and Sydenstricker, E. Pellagra. *Arch. Int. Med.* 1920, **25**, 451, and *Pub. Health Rep., U.S.*, 1920, **35**, 648, 1650, 1701. (*Physiol. Abstr.*, 1920, **5**, 307.)

Eleven white adults (convicts) volunteered in an experiment in which they were fed for months on a monotonous, principally cereal, diet under hygienic conditions. From the second to fifth month symptoms of pellagra occurred in six of them. The remaining convicts, who served as a control, did not get the disease. The second paper contrasts the diet in pellagrous and non-pellagrous households. Increasing supplies of milk or fresh meat decreased the incidence of the disease. No consistent relation, however, was found between varying supplies of maize, wheat, and other foods, and the occurrence of pellagra. The questiom of aetiology still remains open. ‘In reaction to the production of pellagra, the dietary factors to be considered as possibly essential are: (1) an amino-acid deficiency; (2) faulty mineral supply or constitution, and perhaps (3) an as yet unknown (vitamine?) factor. As to which, or what combination or combinations, of these constitute the specific pellagra-producing dietary defects remains to be determined.’ The third paper deals with pellagra incidence in seven cotton mills in South Carolina. The disease is rare in children, is most prevalent April to June, and is less frequent in mill-workers than others, unless the factor ‘disabling sickness’ is taken into account. The fourth paper deals with factors of sanitary importance and in seven mill villages no correlation between these and the incidence of pellagra was found.

C. G. L. W.

Souza, G. de P., and **McCollum, E. V. A study of the factors which interfere with the use of yeast as a test organism for the antineuritic substance.** *J. Biol. Chem.*, 1920, **44**, 113.

The authors regard the Williams yeast test for vitamine as being complicated by too many factors to make it of real value. They claim that many substances other than vitamine may stimulate growth (such, for example, as glucose and amino-acids). As extracts of food are always liable to contain traces of other substances than the vitamine under test, it is clear that any test relying upon a growth stimulation of yeast cells cannot be accurate. R. A. P.

Rosenbaum, S. Über die chemischen Eigenschaften von Nahrungsfuttern verschiedener biologischer Wertigkeit. [**On the chemical properties of food fats of different biological values.**] *Biochem. Ztschr.*, 1920, **109**, 271.

The different biological value of various food fats is well established. The author has attempted to find whether there is any correlation between the value of the food fat and the content of stearin and phosphates without success. R. A. P.

Laqueur, E. Einfluss der künstlichen Füllung der Lunge mit Flüssigkeit, im besonderen durch 'osmotischen Ödem', auf Atmung, Kreislauf und Blut. [**The effect of filling the lungs with fluid, especially oedema fluid, on respiration, circulation, and on the blood.**] *Arch. f. d. ges. Physiol.*, 1920, **184**, 104.

Oedema was induced in rabbits with ligated or divided oesophagus by the injection of 20 c.c. of water or physiological saline solution into the trachea: the effects on respiration, pulse, and blood-pressure were noted. When oedema supervened there was a concentration of the blood proportional to the amount of oedema fluid entering the lungs, as is the case in the oedema of phosgene poisoning. Respirations were increased in frequency but diminished in depth, so that ventilation was unchanged. The reduction in depth was due to reduction in the amount of effective lung tissue, while the increase in rate was regarded as caused by incipient asphyxia. Circulatory effects were also those due to impending asphyxia. Slowing of the rate of respiration by section of the vagi led to death from asphyxia.
C. L. E.

Neuschlosz, S. M. Untersuchungen über die Gewöhnung an Gifte. IV. Die Chiningewöhnung bei Säugetieren. [**Investigations on acquired tolerance to drugs. IV. Tolerance to quinine in mammalia.**] *Arch. f. d. ges. Physiol.*, 1920, **184**, 190.

The estimations of quinine were made by the extraction method of Katz, followed by the titration according to Gordin, and results were accurate to within 3 per cent. When parenterally administered, large doses of quinine can soon be tolerated by dogs and rabbits, and this acquired tolerance is accounted for by an accelerated rate of destruction of quinine in the body. There was no tolerance in oral administration, even in dogs with acquired tolerance to the drug given parenterally. Examination of the press-juices of various organs showed that the normal liver juice, and that of the spleen, kidney, and muscle of accommodated animals has the power of destroying quinine. This property of the organ-juices from tolerant animals is, however, lost if the quinine is first treated with liver extract. The authors think that it can be inferred from this that quinine when given by the mouth is so altered in the liver as to resist further destruction, even by the tissues of accommodated animals. The destruction of quinine in accommodated animals ceases if arsenic is administered, but this is not the case with the (more limited) destruction of the drug by normal animals. The product excreted in the urine after administration of quinine is not quinine, since when isolated and re-administered it is destroyed to a smaller extent than unaltered quinine. C. L. E.

Le Heux, J. W., Storm van Leeuwen, W., u. van den Broeke, C. Quantitative Untersuchungen über den Antagonismus von Giften. II. Näheres über den Antagonismus Pilokarpin-Atropin. [**The antagonism between pilocarpin and atropin.**] *Arch. f. d. ges. Physiol.*, 1920, **184**, 215.

Experiments were made on pieces of surviving rabbit's intestine in Tyrode's fluid supplied with a regular stream of oxygen bubbles; varying concentrations of pilocarpin or mixtures of pilocarpin and atropin were added to Tyrode's fluid and the strips of intestine transferred to these in the desired sequence. The previous experiments of van Lidth de Jeude (*Arch. f. d. ges. Physiol.*, 1918, **170**, 523) were confirmed as regards the relation between the concentration of pilocarpin and its effects, i. e. that the effect was dependent on the concentration of the drug, and not on the total amount present in the solution to which the intestine strip was exposed. The pilocarpin action is completely reversible.

In opposition to the results of van Lidth de Jeude, the present authors find that the antagonistic action of atropin is also dependent on its actual concentration in the solution, and not on the total amount of the drug available. The atropin effect also is completely reversible, at all events as regards doses of moderate size. A portion of surviving intestine, when exposed to a minimally effective concentration of atropin, removes from the solution so little of the drug as to leave the solution unchanged as regards its physiological effects. The curve relating the effect of a pilocarpin solution to its concentration rises at first steeply, and then more slowly, and finally runs parallel to the abcissa, i. e. further increase of concentration is without effect. For concentration of pilocarpin well below that required for the maximal effect, the amount of atropin needed to antagonize does not depend on the concentration of pilocarpin present, but chiefly on the effect which the pilocarpin has produced. Thus the amount of atropin needed to remove a submaximal pilocarpin contraction is three times as great as that needed to remove the effects of a dose which just produced a small contraction. C. L. E.

Voegtlin, C., and Smith, H. W. Quantitative studies in chemotherapy. III. The oxidation of arsphenamin. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 199.

Arsphenamin (dihydrochloride) is exceedingly stable towards atmospheric oxygen. Addition of alkali leads to a rapid increase in the rate of oxidation of the compound, the increase being roughly proportional to the hydroxyl-ion concentration.

Neoarsphenamin shows a rapid oxidation on exposure to air. The nature and rate of oxidation of arsphenamin and neoarsphenamin to the corresponding oxides furnish an explanation of the increase in toxicity and trypanocidal activity of these compounds, when their solutions are exposed to air. H. E. R.

Marshall, E. K., jun. The influence of diuresis on the elimination of urea, creatinin, and chlorides. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 141.

Ingestion of large quantities of water causes a great increase in the volume of urine; creatinin is not increased; urea is definitely increased, and chlorides are apparently increased, but the increase is variable. That the 'no-threshold' substances, creatinin and urea, are not increased equally is contrary to the 'modern theory' of urine secretion suggested by Cushny. H. E. R.

Plant, O. H. The effect of carminative volatile oils on the muscular movements of the intestine. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 311.

Carminative volatile oils increase the muscular movements of the intestine when applied in dilute solution to the mucous membrane of unanaesthetized dogs.

These effects are diminished but not abolished by atropin, but they are abolished when the sensory endings of the mucosa are paralysed by cocaine. H. E. R.

Heinekamp, W. J. R. The action of adrenalin on the heart. III. Modification of the action of adrenalin by chloroform. *J. Pharmacol. & Exper. Therap.*, 1920, **16**, 247.

Chloroform is toxic for heart-muscle. Inhibition after adrenalin under chloroform anaesthesia is due to paralytic dilatation of the heart.

Because of the combined action of these two, adrenalin is contra-indicated during chloroform anaesthesia, or chloroform anaesthesia is contra-indicated after administration of adrenalin. H. E. R.

RADIOLOGY

Radio-technique

Regaud, Cl., et **Ferroux, R.** Constitution rationnelle de tubes-éléments de radium adaptés aux exigences nouvelles de la radiumthérapie. [**Rational constitution of radium tube-elements adapted to the new requirements of radium-therapy.**] *J. de radiol. et d'électrol.*, 1920, **4**, 193.

The 'Dominici' radium tube, consisting as it does of a very small cylindrical platinum sheath containing radium sulphate and the modern flat applicator, represents a great advance in radium therapy. The chief imperfection of both lies in their immutability. The plaque, used as it is for surfaces of varying forms and dimensions, is being replaced by X-rays. A radium tube, although susceptible of more varied use, is good only for certain cases, as it gives a fixed intensity whilst different lesions require widely different intensities.

To realize simplicity of adaptation and precision in dosage and application, the writers consider that the clinician must have a gamut of radium tubes comprising between 20 and 100 microcurie hours of intensity. It would be convenient if the radium content of the tubes was such that the number of microcuries of emanation destroyed per hour was a multiple of 10, or a round number. Experience suggests three series of tubes in which the number of microcuries of emanation destroyed per hour would be 100, 50, and 25 respectively, corresponding to 13·33 mg., 6·66 mg., and 3·33 mg. of radium metal. The exterior lengths and diameters of the platinum tubes for the respective series would be 30 mm. and 1·8 mm., 28 mm. and 1·2 mm., 15 mm. and 1·2 mm. respectively.

The tube-elements of any series may be used in any of the following ways:

(1) As bare tubes for the treatment by puncture of radio-sensitive and voluminous tumours—for example, cancer of the breast.

(2) In groups enclosed in a cylindrical platinum sheath serving, with a supplementary cylindrical platinum filter, for the treatment of cancer of the uterus and rectum.

(3) In groups encased in a metal dish, shaped as required, to form flat applicators.

The weakest series tubes are appropriate for the treatment of epidermoid cancer by radium puncture and for the formation of flat applicators. Those of the 50 $\mu c.\delta$ series are suitable for the treatment of thick tumours by puncture and the production of powerful applicators by grouping several tubes together, whilst the 100 $\mu c.\delta$ serve for uterine cancer.

The constancy of the radiation of such tube elements, particularly those very small tubes of the weakest series, renders them as advantageous as the emanation tubes. For a long application of a weak intensity the advantage is likely to remain with the radium tube. For private practice the radium tube appears preferable to the emanation tube, if the former be modernized on the lines suggested, whilst for a hospital each type has its place.

L. H. C.

Radio-diagnosis

Laquerrière et **Delherm.** Les fractures isolées de la cupule radiale. [**Fractures at the elbow involving the head of the radius only.**] *J. de radiol. et d'électrol.*, 1920, **4**, 337.

The authors here deal only with those fractures of the head of the radius (unassociated with any other lesion of the elbow) where a large fragment is separated. Such fractures are very rare. They may be complete or incomplete, and either variety may be due to direct or indirect violence. Most commonly they result from a fall upon the hand with the arm in extension, in which position the external condyle of the humerus strikes against the anterior part of the head only. The mechanism of fracture by direct violence seems to be either that the head of the radius is driven against the humerus, or that while resting upon the ground it is fractured by the humerus coming down upon it. In either case, and whether the fracture be complete or incomplete, the line of fracture runs diametrically across the superior surface of the head of the radius and passes obliquely downward and outward, delimiting a wedge-shaped fragment upon the outside of the bone.

Clinically the signs are slight and suggestive of a severe sprain. The diagnosis rests upon a marked restriction or complete loss of the rotary movements of the forearm, all attempts at such movements being extremely painful. Flexion and extension of the elbow are relatively little affected and practically painless. There is but little swelling of the elbow, which is held semiflexed with the forearm slightly pronated. The head of the radius may appear slightly enlarged. It is owing to the relatively slight signs that many of these injuries to the head of the radius are missed clinically, and in fact the diagnosis can only be made upon the radiographic findings, the slighter lesions requiring careful scrutiny of the plates for their detection. The authors make a plea for the routine radiography of all injuries to the elbow, when they believe that these fractures will be found to be less exceptional than is supposed, and to be a cause of those cases of persistent arthritis of the elbow following upon a trauma which clinically did not seem to involve any bone.

A brief account of two cases is given, and this is illustrated by radiographs depicting the different types of fracture. E. M. W.

Delherm et **Thoyer-Rozat.** L'image radiologique de l'aorte. Son trajet—ses rapports—son calibre. [**The radiology of the aorta: its course, relations, and calibre.**] *J. de radiol. et d'électrol.*, 1920, **4**, 97.

The work done by the authors on the position and course of the aortic arch was inspired by that done by Cerné in 1913, Mougeot in 1918, and Bordet in 1919. Their observations were made upon the injected cadaver, the following precautions being taken:

(1) Relatively young subjects were used in whom there was no thoracic deformity and whose clinical history was free from any suggestion of a disorder of the circulatory system.

(2) Any dissection involving the region under investigation was avoided.

(3) The subject was examined in the upright position and according to the usual routine of the radioscopic examination of the thorax.

A complete examination under the same conditions was made of three different subjects and orthodiascopy and stereoscopy were used in making records.

Of the great vessels in the mediastinum only one is normally visible in a radiological examination—this is the aorta, and it is visible only in the early part of its course, viz. from the heart to the beginning of the descending aorta. Therefore if the diameter of the visible aorta is to be determined with any accuracy the meaning of the various indefinite and doubtful shadows in the mediastinum must be as far as possible determined. With this end in view the authors extended their inquiry to include the investigation of the injected pulmonary artery and superior vena cava. The results obtained were correlated with clinical findings and the following conclusions drawn:

(*a*) The diameter of the aorta can be measured with accuracy only in the oblique positions—that of the ascending aorta only in the right anterior oblique at an angle of rotation of about 30°, and that of the transverse aorta only in the left anterior oblique at an angle of about 40°. These measurements should correspond in the normal aorta and are to be checked against one another.

(*b*) the best position for viewing the pulmonary artery, which is sometimes very faintly visible, is the left anterior oblique, where it occupies a position at the side of the ascending aorta and within the loop described by the aortic arch.

(*c*) the course of the superior vena cava is behind, to the right of, and parallel to that of the ascending aorta, and in the injected subject is best seen in the right anterior oblique position at an angle of rotation of about 50°.

Numerous diagrams are given illustrative of the situation of the shadows of the different vessels in positions of various degrees of rotation to left and right. E. M. W.

Moreau, L. Les fractures méconnues de la rotule. [**Unrecognized fractures of the patella.**] *Presse méd.*, 1920, **38**, 374. (*J. de radiol. et d'électrol.*, 1920, **4**, 418.)

Fractures of the patella are much more frequent than is indicated by statistics, because many are unrecognized. To avoid mistakes it is necessary to radiograph all traumatisms of the knee; and to obtain the best image of the patella, the latter must be placed in contact with the plate, by compressing the popliteal cavity with the localizing cone. The author also recommends Laquerrière's and Pierquin's technique for obtaining a longitudinal projection of the patella and for bringing its posterior aspect into evidence.

The line of fracture may be in various positions. Usually it is oblique, dividing the patella into two parts, viz. the angle and a part of the base. This type of fracture is often confused with an anomaly of ossification (patella bi-partita) in which there are two bony nodules separated by a thin band of fibrous tissue. Differential diagnosis is sometimes very difficult. In the case of an old fracture there will be nothing to notice, neither pain, nor a notch on palpation. In anomalous cases, the negative may show, instead of a clearly defined line of fracture, irregular osseous edges, jagged, and ill-defined, with appearances of callus in places. But accessory nodules of ossification are found at the supero-external angle, and comparative radiography of the opposite side will reveal the same disposition; nevertheless, in exceptional cases the condition may not be bilateral, as in the case of some sesamoids or supernumerary bones. S. U. L.-B.

Nové-Josserand et **Rendu.** La sacralisation de la V^e lombaire et les accidents qui en résultent. [**Sacralization of the 5th lumbar vertebra and the accidents to which it gives rise.**] *Presse méd.*, 1920, **52**, 514. (*Arch. d'électric. méd.*, 1920, **28**, 282.)

'Sacralization of the fifth lumbar' is the term applied to this vertebra when it shows a tendency to resemble a sacral vertebra in the exaggerated development of its transverse processes. Surgeons had previously drawn attention to this malformation, but its anatomical features were first shown by radiography. The transverse processes lengthen and widen, then spread out into the shape of a butterfly wing. In more marked cases they come into contact with the sacrum or with the dorsum ilii, with which they articulate or become united; indeed they may become so completely fused with the sacrum as to form veritable sacral wings. It is noteworthy that, according as sacralization is more marked, the sacrum becomes shorter, thus raising the question whether lumbarization of the 1st sacral takes place, rather than sacralization of the 5th lumbar. The 19 radiographs collected by the authors show 6 bilateral symmetrical sacralizations, 8 asymmetrical, 6 unilateral, some on the right side and some on the left.

Pain, which is the chief clinical symptom of sacralization, is not continuous and the malformation may remain latent for an indefinite period. Pain is felt towards the base of the sacrum, but irradiations may be directed towards the sciatic, the ischium, the coccyx, and even towards the flanks. In bilateral sacralization, there are anatomical deformations consisting of a flattening of the back with an increase in the transverse dimensions of the sacrum; in unilateral sacralization they consist of lumbar scoliosis and clear asymmetry of the sacro-iliac region.

In spite of radiography, if the patient has not been examined sufficiently long, great care must be taken before establishing the diagnosis and especially the pathogenesis of the pains complained of by the patient. These pains, contrary to the belief of American surgeons, have not always a mechanical origin, and resection of hypertrophied transverse processes in certain cases did not give the expected results. Surgical intervention, therefore, should not be advised absolutely, except in serious cases of progressive neuritis.

Treatment of this affection is not clearly established; improvements have been effected both by surgery and by electro- and radio-therapy, but the results were not absolutely convincing. S. U. L-B.

Radio-biology

Lazarus-Barlow, W. S. On some pathological effects of exposure to the gamma rays of 5 grm. of radium bromide. *Proc. Roy. Soc. Med.*, 1920, **14** (Section of Pathology), 1.

In this paper the author gives a summary of the results of an investigation upon the pathological effects of the gamma rays upon a variety of animals. The source of the gamma rays was approximately five grammes of radium bromide, this quantity being placed at the disposal of the Middlesex Hospital for investigation purposes through the courtesy of the Medical Research Council. The investigations outlined in this paper were supplementary to the clinical investigation in the treatment of malignant disease carried out with the same quantity of radium. In the current Annual Report of the Medical Research Council it is pointed out where in many particulars a strict parallelism has been observed between the action of the gamma rays upon human beings and upon the lower animals. The effects with which the author deals in this paper are those subsequent to a prolonged exposure to gamma rays; the animals dealt with were frogs, rats, rabbits, and cats. It is possible to kill these animals by irradiation alone, the continuous exposure of a rat for forty-five hours causes its death, but a rat exposed for only twelve hours will generally die within about two days. A large difference was observed between the susceptibility of cold- and warm-blooded animals, for the frog supported from twelve to twenty times as much gamma radiation as the other animals dealt with; the cats appeared rather more susceptible than the rats and rabbits.

The cytological changes throughout these irradiated animals have been made the subject of an exhaustive study, the main results of which are grouped in three sub-sections. Regarding the effects upon cell nuclei we read: 'The nucleus may stain faintly and diffusely (endothelium), deeply and diffusely (spermatogonia), faintly and with a few dust-like particles of chromatin (striated muscle), moderately and with a single large nucleolus and a few particles of chromatin (liver), faintly and with a few relatively large particles of chromatin (kidney). In many cases it is impossible to determine whether the appearances are normal, but in some cases it is certain that the nucleus is abnormal. It may be converted into an empty sac (columnar cells of intestine), or may be irregularly vacuolated (striated and unstriated muscle, bone-marrow), or may be 'ghost'-like (liver, kidney, muscle), or the nuclear membrane may have disappeared leaving only a small constellation of chromatin points (kidney, liver), or the entire nucleus may have become broken up into deeply-stained débris (lymphocytes, intestinal mucosa), or, finally, all traces of a nucleus may be lost, though cytoplasm persists (liver, kidney). In the case of neoplasms, any of these appearances may be met with, but most frequently the chromatin is gathered into an irregular mass situated more or less in the middle of an enlarged, irregular, and often vacuolated spheroid.

In analogous detail we find for the effects upon the cytoplasm of the cell: 'The cytoplasm may be hyaline and basophil, oxyphil or indifferent (pancreas), translucent and oxyphil (gastric mucosa), vacuolated (bone-marrow, kidney, unstriated muscle), or it may be converted into mucus (intestine, trachea), or show fine granules (salivary gland), or globules of lipoid (adrenal, convoluted tubules of cat), or, rarely, it may show neutral fat globules (tracheal cartilage, paraortic tissue of rat, kidney of cat). Of these modifications the intense mucoid change in intestine and the lipoid change in kidney of cat will be referred to later. But perhaps the most striking change of cytoplasm seen after exposure to a large quantity of radium is its complete disappearance. In this case the nucleus is left suspended, as it were, in the middle of a cavity limited, at some distance, by the cell membrane which, now, is unusually conspicuous. Since the condition is most marked in animals that have survived for some days, after a somewhat severe exposure, this disappearance of cytoplasm must be regarded as secondary.' After long exposures, there are profound changes in the blood, both upon the red corpuscles and upon the leucocytes, the general trend of the observations being rather similar to those of investigations with X-rays.

The organs chiefly dealt with in the remainder of the paper are the muscular system, where differences were observed in the changes undergone by voluntary, involuntary, and cardiac muscle; the liver; the kidney, in which striking changes were met with in the convoluted tubules of the irradiated cat; and, finally, the generative system. Despite the well-known fact that the testicle and ovary are very vulnerable to X-rays, no profound changes in these organs were observed after prolonged exposure to the radium; this is, as the author remarks, probably to be explained by the short survival of the animal after these massive irradiations. A complete cessation of mitosis was, however, observed in the testicle after such irradiation. The paper is illustrated by four microphotographs. Apart from the bearing and value of many of the observations upon the radiological treatment of disease in man, the data provide most abundant evidence for the essentially selective action of the gamma rays upon tissues. As more studies become directed upon this subject the field of investigation becomes wider and wider, and the terms which hitherto have served no longer suffice. It is not sufficient to recognize that there are differences in vulnerability between striated and unstriated muscle, for we read in the section of the paper devoted to the muscular system, 'it was somewhat surprising to find that differences obtained even in the single group of striated or unstriated muscles. And it was even more surprising to find that normal bicipital muscle, for example, may generally be diagnosed from abdominal muscle by the relative shortness and thickness of its nuclei.'

The paper is a communication which will repay the closest perusal by radiologists and pathologists who desire to know more of the effects of these radiations upon living tissues. S. R.

Radium Therapy

Shaw, W. F., and Burrows, A. Wertheim's hysterectomy for advanced carcinoma of the cervix made possible by the use of radium. *Proc. Roy. Soc. Med.*, 1920, **13** (Section of Obstetrics and Gynaecology), 191–8.

The greatest advance in the treatment of carcinoma of the cervix is Wertheim's operation; the chief cause of failure is the late stage at which the gynaecologist is consulted. Radium has a marked action on carcinoma of the cervix. Many cases were treated, a large percentage showed marked improvement; in many the disease had apparently disappeared locally two months after the application, but in no case did the improvement last more than a year. Fourteen cases in all were operated upon, which were too advanced for operation when first seen, but became operable two months after the application of radium. In six the operation was abandoned as it was impossible to separate the ureter or bladder from the hard cartilage-like tissue which replaced the growth. Two cases had recurrence, a few months and during the second year after operation, and one patient died from the effects of the operation. The remainder are well.

The only difficulty in the operation is the presence of hard cartilaginous material in place of the original growth.

Every case was diagnosed as 'inoperable carcinoma' by Shaw, and tubes were inserted by Burrows after examination. Shaw states that radium does definitely increase the operability in this type of case, but no precise figures are given.

Methods of administration of radium are dealt with by Burrows.

The main points in treatment are:

(1) Many tubes must be buried in the cervix and surrounding tissues.

(2) The largest possible dose must be employed.

The large number of tubes allows a big dose to be given with the least focal necrosis, and therefore a greater power of healthy regeneration of the tissues. Pointed tubes of platinum $\frac{3}{10}$ mm. thick, containing emanation, were used with a larger central silver screened tube up the cervical canal towards the upper end of the growth.

No uniformity of good results can be obtained with less than 120 mg. of radium or millicuries of emanation for twenty-four hours. The growth must be cleaned before treatment and douched daily for six weeks after to prevent vaginal adhesions. To indicate the use of radium in carcinoma of the cervix, details were given of 150 cases, all regarded as inoperable before the application of radium, of which nearly 20 per cent. were operated upon after radium treatment. P. L.-B.

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